

Delay between the onset of symptoms of acute myocardial infarction and seeking medical assistance is influenced by left ventricular function at presentation

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Abstract

Objective—To determine whether the interval between the onset of symptoms of acute myocardial infarction and the patient's call for medical assistance (patient delay) is related to left ventricular function at the time of presentation.

Design—Prospective observational study.

Setting—Coronary care unit of Aberdeen Royal Infirmary.

Patients—93 consecutive patients with acute myocardial infarction.

Main outcome measures—Left ventricular stroke distance, expressed as a percentage of the age predicted normal value, measured first on admission, and then daily for 10 days or until discharge. Patients were questioned at admission to determine the time of onset of symptoms and the time of their call for medical assistance.

Results—Median (range) patient delay was 30 (1-360) min. Mean (SD) stroke distance on admission was 70(18)%, rising to 77(19)% on the second recording, and to 84(18)% on the day of discharge. Linear regression of $\log_e(\text{patient delay})$ against first, second, and last measurements of stroke distance gave correlation coefficients of 0.28 ($P < 0.01$), 0.18 (not significant), and 0.11 (not significant), respectively.

Conclusions—Patient delay within the first 4 h after the onset of symptoms of acute myocardial infarction is positively related to left ventricular function on admission. A possible explanation is that deteriorating left ventricular function influences the patient's decision to call for help. This tendency for patients with more severe infarction to call for help sooner is an added reason for giving thrombolytic treatment at the first opportunity: those who call early have most to gain from prompt management.

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Keywords: acute myocardial infarction; left ventricular function; patient delay

The interval between the onset of symptoms of acute myocardial infarction and the patient's call for medical assistance (patient delay) varies widely, and the variance is

mostly unexplained by demographic or sociological factors,^{1,2} although psychological factors may be important.^{3,4} Attempts to shorten patient delay by public education have generally not been successful,⁵⁻⁷ and patient delay is no different in those with or those without a previous history of myocardial infarction.⁸⁻¹⁰ The failure of such educational efforts, and the demonstration that patient delay is not altered by the previous experience of myocardial infarction, challenge the underlying assumption that patient behaviour during myocardial infarction is learned and culturally determined.

We have previously shown that patient delay is influenced by the severity of infarction, as reflected by aspartate aminotransferase concentrations and the risk of ventricular fibrillation and death.^{9,10} The more severe the infarction, the greater the degree of pain assessed by visual analogue scores, and the shorter the patient delay. The initiation of a call, however, is still largely unexplained in terms of worsening symptoms. This suggests that patients may be responding to other stimuli that do not reach consciousness during infarction, such as those resulting from deteriorating left ventricular function.

In this study patient delay in those with acute myocardial infarction was correlated with left ventricular function assessed on admission and subsequently.

Patients and methods

SELECTION OF PATIENTS

A total of 150 consecutive patients presenting to the coronary care unit with suspected acute myocardial infarction between 7 00 am and 11 00 pm were examined. Of 145 patients in whom left ventricular function was satisfactorily assessed, 93 had acute myocardial infarction, and are the subjects of this study.

The diagnosis of acute myocardial infarction was made if any two of the following were present: a history of characteristic chest pain lasting more than 30 min, development of new Q waves on the electrocardiogram, or an increase in the concentration of cardiac enzymes to at least twice the upper limit of normal.

The mean age of the patients was 62. A history of previous myocardial infarction was present in 15, and 76 were given thrombolytic treatment; none was treated with a β blocker or an angiotensin converting enzyme inhibitor on presentation.

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ASSESSMENT OF LEFT VENTRICULAR FUNCTION

Left ventricular function was assessed as stroke distance, the systolic velocity integral of blood flow in the aortic arch,¹¹ the case for considering stroke distance as a measure of left ventricular function has been argued elsewhere.^{12,13} Stroke distance was measured using a Doptek spectrum analyser (Doptek, Chichester, West Sussex) with a 2 MHz continuous wave ultrasound probe directed at the aortic arch through the suprasternal window. Mean stroke distance was averaged from as many beats as were stored in a 10 s sequence, evaluated by on-screen planimetry. The reproducibility of this technique in our hands is 7–9%.^{13,14} The results are expressed as percentages of age predicted normal values.¹⁵ Measurement of stroke distance was attempted in 150 patients and satisfactory recordings made in all but five: three patients had cardiogenic shock and died, and two had chronic obstructive airway disease.

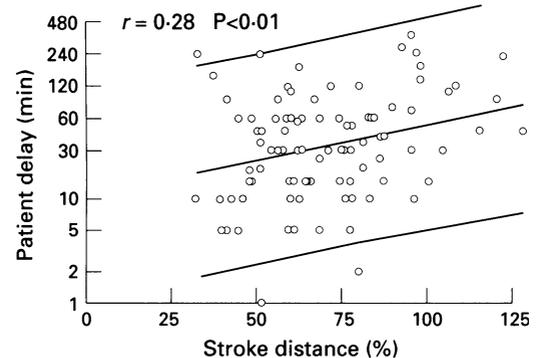
The measurement of stroke distance was made at the patient's bedside as soon as possible after admission, usually just before, but never more than 15 min after, the start of thrombolytic treatment. Further measurements of stroke distance were made daily for 10 days, or until discharge.

DOCUMENTATION OF TIME DELAYS

At the time of the first stroke distance measurement patients were questioned to establish the time of onset of symptoms and the time of their call for help, either to their general practitioner or for an ambulance. The times of admission, first measurement of stroke distance, and starting thrombolytic treatment were also noted.

STATISTICAL ANALYSIS

Time delays had a skewed distribution which was normalised by logarithmic transforma-



Relation between first measurement of stroke distance and patient delay in 93 patients with acute myocardial infarction. Regression line and 95% confidence intervals are shown.

tion, as was the maximum recorded concentration of aspartate aminotransferase. Linear regression of $\log_e(\text{patient delay})$ against haemodynamic variables was performed. Student's *t* test was used for comparison of means; Wilcoxon's test was used for comparison of medians. Statistical significance was defined as $P < 0.05$.

Results

TIME DELAYS

Table 1 gives time delays for all patients and for the 76 who were given thrombolytic treatment. Median patient delay for all patients was 30 min; the longest delay was 6 h, but in only two patients was it more than 4 h.

STROKE DISTANCE

Mean (SD) stroke distance on admission was 70(18)% rising to 77(19)% on the second recording ($P < 0.001$), and to 84(18)% on the day of discharge ($P < 0.001$). These values were almost identical in the 78 patients without a history of previous infarction.

REGRESSION ANALYSES

Table 2 lists the correlation coefficients for linear regression of $\log_e(\text{patient delay})$ against various haemodynamic variables and $\log_e(\text{maximum aspartate aminotransferase})$ concentration for all patients and those with no history of previous infarction. The strongest association is between patient delay and stroke distance on admission in patients with no history of previous myocardial infarction. The association between patient delay and stroke distance is stronger with the first than with subsequent measurements. The figure shows the relation between admission stroke distance and patient delay.

Discussion

PATIENT DELAY

Median patient delay in this series of patients with acute myocardial infarction was 30 min, which is shorter than in previous reports.^{9,10} This need not indicate any recent change in patient behaviour, but is more likely to be explained by the method of selection of cases for admission to the coronary care unit and

Table 1 Time delays in all patients and in those who received thrombolytic treatment

	Median	Range	Mean
All patients (n = 93)			
Patient delay	30	1–360	58
Call to door	100	22–754	130
Door to first measurement of stroke distance	20	0–145	24
Call to first measurement of stroke distance	125	30–780	154
Onset to first measurement of stroke distance	175	67–790	213
Thrombolytic treatment (n = 76)			
Patient delay	30	1–240	
Call to door	100	22–640	
Door to injection of thrombolytic agent	20	0–125	
Call to injection of thrombolytic agent	120	35–690	
Onset to injection of thrombolytic agent	155	70–720	

Table 2 Correlation coefficients for regression of $\log_e(\text{patient delay})$ against haemodynamic variables and $\log_e(\text{maximum aspartate aminotransferase})$

	Patients with no history of myocardial infarction (n = 78)		All patients (n = 93)	
	r	P	r	P
Admission stroke distance	0.32	< 0.01	0.28	< 0.01
Second stroke distance	0.23	< 0.05	0.18	< 0.10
Discharge stroke distance	0.16	< 0.25	0.11	> 0.25
Admission minute distance	0.17	< 0.25	0.18	> 0.10
Admission heart rate	-0.16	< 0.25	-0.08	> 0.25
Admission systolic blood pressure	-0.12	> 0.25	-0.02	> 0.25
$\log_e(\text{maximum aspartate aminotransferase})$	-0.13	> 0.25	-0.17	< 0.25

entry to the study. Median delay is critically dependent on whether there is an upper time limit for entry. Although none was formally set, patients presenting late may be less likely to be admitted to the coronary care unit. Conversely, younger patients with ST segment elevation may be preferentially admitted. These factors are associated with shorter patient delay.¹⁶⁻¹⁸

STROKE DISTANCE

Mean stroke distance rose from 70% on admission to 77% on the second recording, and to 84% at discharge. These values are similar to those in two previously published series in which daily improvements in stroke distance were documented in patients with acute myocardial infarction.^{11,19} The present study differs from the others in that stroke distance was first measured a few minutes after admission, rather than several hours afterwards on the first morning. Mean stroke distance on admission is lower than has previously been reported in patients with acute myocardial infarction, and the largest daily increment in mean stroke distance occurred between the first and second measurements. This is most probably the result of successful reperfusion after thrombolytic treatment, which was given to the majority of patients. Second and subsequent measurements of stroke distance will therefore be influenced by the extent of recovery of left ventricular function, either spontaneous, or after intervention. By contrast, admission stroke distance is likely to reflect severity of infarction, as none of the patients received thrombolysis before hospitalisation.

RELATION BETWEEN PATIENT DELAY AND STROKE DISTANCE

There is a modest but significant ($P < 0.01$) positive relation between patient delay and stroke distance recorded on admission. The association with patient delay weakens with second and subsequent measurements of stroke distance, so that it is not statistically significant by the time of discharge. The nearer one approaches the patient's decision to call for help, the stronger the association between patient delay and left ventricular function; the association is strongest in patients without previous myocardial infarction. It is difficult to conceive of a mechanism whereby greater delay in the patient calling for help results in less severe infarction and better left ventricular function, but a causal connection in the opposite direction, between left ventricular function and patient delay, is not unlikely.

We have previously shown a negative relation between peak aspartate aminotransferase concentration, indicative of infarct size, and patient delay ($r = -0.2$, $P < 0.01$, $n = 250$),¹⁰ and such a relation has been reported by others.²⁰ A similar association was found in the present study ($r = -0.17$, $P < 0.25$, $n = 93$). The problem is to explain how patients' behaviour is affected by infarct size, of which they would have no direct knowledge at the

time of the decision to call for help. The severity of pain is only partially related to patient delay, while the symptoms of anxiety and breathlessness are unrelated.¹⁰ Our results indicate that the relation between patient delay and left ventricular function is stronger than the relation between patient delay and peak cardiac enzyme concentration. This suggests that it is not infarct size itself, but its effect on left ventricular function that influences the decision to call for help. There remains the problem of how patients know that their left ventricular function is impaired when breathlessness is not a predominant symptom. Direct stimulation of the autonomic nervous system through cardiac receptors may be the mechanism.^{21,22}

The relation between patient delay and left ventricular function that we have demonstrated goes some way towards explaining our previous findings of a negative relation between severity of infarction and patient delay for delays of up to 4 h.^{9,10} Our results are consistent with those from Western Washington where patients with acute myocardial infarction presenting to hospital within 2 h of onset were more likely to have cardiogenic shock or hypotension.²³

IMPLICATIONS FOR THE INTERPRETATION OF CLINICAL TRIALS

The efficacy of thrombolysis has been demonstrated in several large placebo controlled trials. Some of these,^{24,25} although not all,^{26,27} have reported increased benefit with earlier administration, as would be expected theoretically. Where this "time-effect" has been demonstrated, its magnitude has not been great. In these trials, however, thrombolytic treatment was given in hospital at the first opportunity, and patient delay would have constituted a substantial proportion of the total delay to the start of treatment, especially when thrombolysis was started early. The outcome in patients treated at different times within the first 4 h after the onset of symptoms of acute myocardial infarction is the result of two opposing influences, namely, the greater severity of infarction with earlier presentation and the greater efficacy of treatment with earlier administration. The benefit of early treatment is therefore underestimated because of the tendency for patients with more severe infarction to present earlier. Because the composition of patient groups presenting at different times will vary, it is erroneous to estimate the magnitude of the time effect by comparing mortality reduction at different times of administration in placebo controlled trials.^{28,29} The magnitude of the time effect can be determined only by clinical trials in which patients are randomly allotted thrombolytic treatment at the first opportunity, or after a deliberate delay^{30,31}; the additional benefit from earlier treatment may be substantial.³²

IMPLICATIONS FOR CLINICAL PRACTICE

The victim of acute myocardial infarction is faced with a novel, life threatening predicament, to which there may be an instinctive

response, at least to those stimuli that are subliminal; individuals with greater somatic awareness and pain perception may seek earlier assistance.³ It seems, therefore, unlikely that behaviour at this time can be readily changed: patients targeted by schemes of public education, where the level of instruction is necessarily brief and superficial, have not shown any lasting reduction of decision times.⁵⁻⁷ By contrast, American physicians with myocardial infarction demonstrated less delay than American patients in ISIS-2.³³ Perhaps it should now be acknowledged that patient delay is unlikely to be changed by anything less than intensive training, and that resources used on public education might be better used elsewhere.

Most patients (84 of 93) in this study were directly referred by their general practitioners to the coronary care unit, where the door to injection of thrombolytic agent time was short (20 min). Nevertheless, the 2 h call to injection of thrombolytic agent time was twice as long as the ideal recommended by the British Heart Foundation,³⁴ and only one quarter of patients (19 of 76) received thrombolytic treatment within 2 h of the onset of symptoms and none within 1 h. This contrasts with the Grampian region early anistreplase trial, in which almost two thirds of those randomised to domiciliary thrombolysis received treatment within 2 h, and the median call to injection of thrombolytic agent time was 55 min for home treatment.³⁰

Although it may be difficult to shorten patient delay, the tendency for less delay in those with more severe infarction and impaired left ventricular function works to the patients' advantage provided that there is a rapid and effective response for assistance. It is an added reason for administering thrombolytic treatment at the first opportunity: those patients who seek medical care early have most to gain from prompt, effective management.

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