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Repeat thrombolysis for acute myocardial infarction

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Abstract

Background: Thrombolysis is still the first line of treatment for acute myocardial infarction in the United Kingdom. In a significant proportion of these patients thrombolytic therapy fails to restore patency of the occluded artery or is followed by early re-infarction. The best management of this group of patients is not clear although repeat doses of thrombolysis are commonly administered especially in the district general hospitals that do not have access to invasive facilities. We performed a retrospective clinical study to determine the outcome of repeat thrombolysis for acute myocardial infarction in patients with failed initial thrombolysis or early re-infarction.
Methods: Ninety-two patients who received two or more doses of thrombolysis for acute myocardial infarction were compared with 98 contemporary similar patients who received only one dose of thrombolysis. Case notes of all patients were examined for retrospective analysis. Main outcome measures were death, heart failure and need for in-hospital revascularization.
Results: Compared to the group thrombolysed once, in the rethrombolysed group there were significantly more deaths at 30 days (p=0.0016), more heart failure (with lower mean ejection fraction), more cardiac arrests as well as more frequent coronary angiography and percutaneous coronary interventions (PCIs). The incidence of haemorrhage in the two groups did not differ.
Conclusions: The need for repeat thrombolysis identifies a group of patients with a high risk of early complications. Although repeat thrombolysis is safe, these patients then need close monitoring with a view to early intervention. For such patients admitted to district general hospitals without interventional facilities early referral to a tertiary center should be considered.

Keywords: Repeat thrombolysis; Acute myocardial infarction; Heart failure

1. Introduction

The treatment of acute myocardial infarction (MI) with thrombolysis fails to achieve patency of the infarct related artery in 15–40%cases [1–4]. In those that reperfuse 10% will reocclude while still in the hospital [5–8]. Angiographic failure to reperfuse is associated with a higher incidence of early death, greater left ventricular dysfunction and overall a worse prognosis compared to those that reperfuse [9–12]. It is not clear what the best management should be in this large group of patients where primary thrombolytic therapy has failed. In the United Kingdom, at the moment, the management approach lies between a conservative approach (supportive treatment), repeat thrombolysis or rescue percutaneous coronary intervention (PCI) [13,14]. The availability of local hospital facilities often dictates management with conservative management or further thrombolysis being chosen where on-site cardiac catherization facilities are not available. Repeat thrombolysis is frequently used for failed thrombolysis although evidence to favour this practice is not strong [15–19]. A retrospective analysis of the treatment strategies employed on patients with early reinfarction in the GUSTO 1 and ASSENT 2 thrombolytic trials, however, demonstrated benefit of repeat thrombolysis over conservative treatment with antithrombotics and vasodilators [20]. In order to assess the outcome of repeat thrombolysis, as well as to investigate what important differentiating features separate successful from unsuccessful thrombolysis, we retrospectively studied a group of

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patients thrombolysed two or more times in the same hospital admission for acute myocardial infarction and compared them with a similar group that was thrombolysed only once.

2. Materials and methods

Between April 1997 and April 1998, 548 patients were admitted to the coronary care unit at Hull Royal Infirmary with a diagnosis of possible acute myocardial infarction. Of these 484 were eligible for thrombolysis. From this population, all of whom received thrombolysis for acute MI, we were able to identify 92 patients who received two or more doses of thrombolysis for failed reperfusion or reinfarction during the same hospital admission (group A). This group was compared with a contemporary and randomly selected group of 98 patients of acute MI that received only one dose of thrombolysis in that hospital admission (group B).

Acute myocardial infarction was defined as the presence of at least two of three characteristics: ischaemic cardiac pain for >30 min, ST segment elevation of ≥1 mm in two or more leads or ST depression of at least 2 mm with tall R waves in V1–V3, and significant rise in cardiac enzymes (elevated creatine kinase [CK] with MB fraction 4% or more of total CK). The MIs were labelled anteror, inferior and 'other' based on ECG findings. 'Other' included lateral and true posterior wall MIs. No MIs presented with left bundle branch block (LBBB) in the time frame of our study. Failure of reperfusion was defined as less than 50% resolution of ST segment elevation at 90 min following the start of thrombolytic therapy. If at 90 min the patient was pain-free with greater than 50% resolution of ST segment elevation but later developed recurrent chest pain with further progressive ST elevation this represented reinfarction. All patients were initially thrombolysed with streptokinase (1.5 million units intravenously over 1 h). Repeat thrombolysis was with intravenous rt-PA (15 mg bolus, followed by 50 mg over 30 min, followed by 35 mg in 1 h) in all cases.

Previous angina was defined as a history of exertional chest pains suggestive of angina occurring 48 h or more prior to the presentation with the MI.

Serum CK was measured on admission and again 12 h after thrombolysis. Left ventricular ejection fraction (EF) was available on all patients and measured either by echocardiography prior to discharge from the hospital or by radionucleide ventriculography within 4–6 weeks of discharge.

Heart failure was defined as the presence of clinical signs of heart failure (S_3 gallop, basal rales, elevated jugular venous pressure, ankle oedema) along with pulmonary oedema on the chest X-ray or either of these alone.

Bleeding not requiring transfusion or fluid resuscitation was defined as minor haemorrhage. Haemorrhagic stroke was diagnosed as the development of new neurological signs during or within 24 h after thrombolysis with confirmation of intracranial bleeding on a CT head scan. Mortality was assessed at 30 days.

The differences between groups were assessed by using Student's *t*-test for continuous variables and χ^2 test (with Yates' correction as appropriate) for categorical variables.

Cox-proportional hazards analyses were used to assess prognostic associations. The hazard ratio (RR) with 95% confidence intervals (CI) and *p*-values by the likelihood-ratio test are given. Hazard ratios for continuous variables apply per unit of the analysed variable. Kaplan–Meier cumulative survival plots were constructed to illustrate the difference groups.

3. Results

3.1. Patient characteristics

Ninety-two and 98 patients were identified in groups A and B, respectively. While uncomplicated, successfully thrombolysed patients were discharged by 5 days, patients with complications stayed in hospital up to a maximum of 1 month. The patient characteristics of the two groups including background history and vascular risk factors are outlined in Table 1. Compared to the group that had single lysis, group A was significantly older and were more likely to have a previous history of angina. Fewer patients in this group were current smokers compared to the single lysis

Table 1
Patient characteristics including background history, risk factors for ischaemic heart disease and details of MI/thrombolysis

Characteristics	Repeat thrombolysis group (*n*=92)	Single lysis group (*n*=98)	*P* value
Mean age	64±13	61±11	0.03
Males	61 (66%)	60 (61%)	0.47
Previous angina	44 (47.8%)	26 (26.5%)	0.002
Previous MI	29 (31.5%)	23 (23.5%)	0.21
Previous CABG	7 (7.6%)	5 (5.1%)	0.07
Previous CVA	4 (4.3%)	6 (6.1%)	0.58
Peripheral vascular disease	7 (7.8%)	5 (5.1%)	0.45
Currently smoking	31 (35.2%)	47 (49.5%)	0.05
Previously smoking	28 (38.4%)	26 (28.9%)	0.05
Hypertension	31 (33.7%)	29 (29.6%)	0.54
Diabetes mellitus	7 (7.6%)	5 (5.1%)	0.48
Family history of IHD	35 (58.3%)	41 (49.4%)	0.29
Elevated admission total cholesterol	59 (75.6%)	69 (75%)	0.92
Anterior MI	46 (50%)	42 (42.9%)	0.32
Inferior MI	48 (52.2%)	54 (55.1%)	0.69
Other MI	4 (4.3%)	2 (2.04%)	0.36
Mean CK rise at 12 h	2153±1686 iu/l	1797±1343 iu/l	0.12
Mean time to 1st thrombolysis	10.6±26.8 h	4.3±4.0 h	0.02