

Myocardial Reperfusion with Streptokinase in an Asian Population with Acute Myocardial Infarction: Analysis of 60-Minute ST Resolution

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CHEN ET AL.: Myocardial Reperfusion with Streptokinase in an Asian Population with Acute Myocardial Infarction: Analysis of 60-Minute ST Resolution. **Aims:** We sought to determine the efficacy of streptokinase in myocardial reperfusion in an Asian population with acute myocardial infarction by using 60-minute ST resolution and the predictors of complete ST resolution. **Materials and Methods:** We conducted a retrospective study on 96 consecutive Asian patients with acute myocardial infarction. All received streptokinase and had interpretable electrocardiograms (ECGs) before and 60 minutes after streptokinase initiation. ST resolution was categorised into three groups: complete ($\geq 70\%$), partial (30% to $< 70\%$) and no (0% to $< 30\%$). Independent predictors of complete resolution were identified by multivariate analysis. The incidence of complete, partial, and no ST resolution was 24%, 27%, and 49% respectively. Independent predictors of complete ST resolution were inferior infarction (OR 7.82; CI 2.58-23.68; $p=0.0003$) and smoking history (OR 5.2; CI 1.42-19.07; $p=0.0147$). In a subgroup of patients ($n=43$) with interpretable ECGs at both 60 and 90 minutes, the incidence of complete, partial and no ST resolution changed from 12%, 23%, and 65% to 26%, 44%, and 30% respectively ($p=0.01$). **Conclusion:** Streptokinase restored myocardial perfusion in 24% of an Asian population 60 minutes after initiation. Independent predictors of myocardial reperfusion were inferior infarction and smoking history. The majority of patients without complete ST resolution at 60 minutes did not have successful myocardial reperfusion by 90 minutes without additional intervention. (*J HK Coll Cardiol* 2001;9:133-138)

Acute myocardial infarction, Asians, fibrinolysis, myocardial reperfusion, ST resolution, streptokinase

摘要

目的：通過觀察ST段在60分鐘內的演變情況研究鏈激酶對於患有急性心肌梗死的亞洲患者心肌再灌注的影響及完全的ST演變的預測價值。材料與方法：我們連續對96名患有急性心肌梗死的亞洲患者進行了回顧性分析。所有患者均用鏈激酶並在用藥前和用藥60分鐘心電圖有變化。根據ST演變分為3組：完全變化（ $\geq 70\%$ ），部分變化（30%– $< 70\%$ ），無變化（0%– $< 30\%$ ）。通過多元分析找出獨立的預測指標。ST段有變化、部分變化和無變化的發生率分別占24%，27%和49%。有完全的ST段演變的獨立預測指標為下壁心梗（OR 7.82；CI 2.58–23.68； $p=0.0003$ ）和吸煙史（OR 5.2；CI 1.42–19.07； $p=0.0147$ ）。在心電圖有演變的亞組病人中（ $n=43$ ），60和90分鐘內ST完全變化、部分變化和無變化分別為12%，23%；65%到26%；44%和30%（ $p=0.01$ ）。結論：鏈激酶在應用60分鐘後可使24%的亞洲患者恢復心肌灌注。心肌再灌注的獨立預測指標為下壁心梗和吸煙史。如果不進行另外的干預，在60分鐘內無完全ST變化的患者大多數到90分鐘時仍無成功的心肌再灌注。

關鍵詞：急性心肌梗死 亞洲人 纖維蛋白溶解 心肌再灌注 ST演變 鏈激酶

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Introduction

Reperfusion therapy using fibrinolytic agents is the standard of care in the management of patients presenting with ST-elevation myocardial infarction. The goal of reperfusion therapy is rapid, complete, and sustained restoration of normal flow in the infarct-related artery (IRA), thereby preserving left ventricular function and reducing mortality. Recent evidence has shown that re-establishment of normal epicardial flow does not mean successful myocardial reperfusion.¹ Despite attaining Thrombolysis in Myocardial Infarction grade 3 flow in the IRA, myocardial reperfusion may still be impaired after primary percutaneous transluminal coronary angioplasty. This is associated with larger infarcts, poor left ventricular functional recovery, and increased mortality.²⁻⁶ Two methods have been developed recently to characterise myocardial reperfusion. The Thrombolysis in Myocardial Infarction myocardial perfusion grade uses the clearance of the myocardial blush on the coronary angiogram to define different grades of myocardial reperfusion.⁷ This angiographic method of assessing myocardial reperfusion involves the performance of an invasive procedure and is not readily available. Resolution of ST elevation on the surface electrocardiogram (ECG) has been shown to correlate closely with myocardial contrast echocardiography findings⁸ and thus is a marker of myocardial reperfusion. Moreover, ST resolution carries prognostic implications in patients with acute myocardial infarction receiving fibrinolytic agents or undergoing primary percutaneous transluminal coronary angioplasty.⁹⁻¹⁵

Although new fibrinolytic agents have been developed and are starting to replace tissue plasminogen activator in the Western population, streptokinase is still used in many parts of the world as the fibrinolytic of first choice in ST-elevation myocardial infarction. Large-scale randomised controlled trials on the efficacy and safety of fibrinolytic therapy in acute myocardial infarction have not been performed on the Asian population. We sought to determine the efficacy of streptokinase, which is more frequently used than tissue plasminogen activator in Asia, in restoring myocardial perfusion in an Asian population with acute myocardial infarction. We assessed myocardial reperfusion by analysing 60-minute ST resolution, and sought to identify the predictors of complete ST resolution.

Materials and Methods

Study Population

We conducted a retrospective study on consecutive Asian patients admitted to the 3 participating institutions (Ruttonjee Hospital, Queen Mary Hospital, and Centro Hospitalar Conde de São Januário) from July 1999 to June 2000 with a diagnosis of acute myocardial infarction. All hospitals are major regional hospitals with an Emergency Department serving a predominant Asian population (>95%). Acute myocardial infarction was diagnosed by ischaemic chest discomfort ≥ 30 minutes in duration and ST segment elevation ≥ 0.1 mV in two contiguous limb leads or ≥ 0.2 mV in two contiguous precordial leads. We limited the analysis to cases in which 1.5 million units of streptokinase were given and 12-lead ECGs before and 60 minutes after the administration of streptokinase were available.

ECG Analysis

ECGs of patients from each institution were analysed by a single investigator of that institution (WHC, PYL & TMM). The method of ECG analysis reported by Schröder et al was used.¹⁶ The magnitude of ST segment elevation was measured manually 20 ms after the end of the QRS complex from leads I, aVL and V1 to V6 for anterior MI and leads II, III, aVF and V5 to V6 for inferior MI. Reciprocal ST depression ≥ 0.1 mV in leads II, III and aVF for anterior MI and in leads V1 to V4 for inferior MI were included. The sum of ST deviation was calculated at baseline and 60 minutes after initiation of streptokinase. Whenever available, measurement was also made at 90 minutes. The percent resolution of ST deviation was calculated and categorised into 3 groups according to Schröder's definition: complete resolution ($\geq 70\%$), partial resolution (30% to $<70\%$), and no resolution (0% to $<30\%$).

Statistical Analysis

Continuous variables were expressed as mean \pm SD and 95% confidence interval where appropriate. Categorical variables were compared using Pearson chi square tests or Fisher's exact test where appropriate. Continuous variables were compared using one-way analysis of variance (ANOVA) (*F* tests). A logistic regression analysis using forward technique was

employed to determine significant independent predictors of complete ST resolution. A significant level was defined when $p < 0.05$. Data were analysed using the SPSS 6 software package (SPSS Inc., Prentice Hall, New Jersey).

Results

The clinical characteristics of the patients are summarized in the Table 1. Among the 96 patients with interpretable ECGs 60 minutes after initiation of streptokinase, 24%, 27%, and 49% had complete, partial, and no ST resolution respectively. When compared with the groups with partial or no resolution, the group with complete resolution had a higher prevalence of a smoking history ($p = 0.027$) and an inferior location of myocardial infarction ($p = 0.0001$). More patients with

complete resolution (91%; versus 62% and 68% for the partial and no resolution groups respectively; $p < 0.05$) received streptokinase ≤ 4 hours after symptom onset. The mean symptom-onset to treatment time was 80 minutes earlier for the complete resolution group compared with the other two groups combined (160 ± 71 minutes versus 240 ± 189 minutes; $p = 0.003$). Almost 80% of the patients with complete resolution had inferior infarction. The reverse was noted in the partial resolution group. More anterior myocardial infarction was also observed among patients with no resolution but of a smaller magnitude ($\sim 60\%$). For patients with inferior myocardial infarction, 83% had a symptom-onset to treatment time ≤ 240 minutes and 59% had a sum of ST deviation ≤ 1.0 mV, compared with 64% and 33% respectively of patients with anterior myocardial infarction. Prior myocardial infarction was less common in the complete resolution group than in the partial

Table 1. Clinical characteristics of patients classified according to ST resolution at 60 minutes after administration of streptokinase. Σ ST Δ = sum of ST deviation before streptokinase infusion

	All	Complete Resolution [n=23 (24%)]	Partial resolution [n=26 (27%)]	No Resolution [n=47 (49%)]	p value
Mean age (y)	65	64	65	66	NS
>65, %	53	52	50	55	NS
Chinese, %	95	100	92	94	NS
Male sex, %	82	91	81	79	NS
Diabetes, %	22	22	31	17	NS
Hypertension, %	36	35	38	36	NS
Hypercholesterolaemia, %	58	70	54	55	NS
Current or ex-smoker, %	65	87	54	57	0.027
Prior MI, %	11	4	27	6	0.014
Heart failure, %	3	0	4	4	NS
Anterior MI, %	58	22	81	62	0.0001
Killip class >1, %	23	13	27	30	NS
Cardiogenic shock, %	7	4	12	6	NS
Mean duration from symptom-onset to treatment, min	241	160	247	237	NS
Time from symptom onset to treatment ≤ 240 min, %	72	91	62	68	0.0497
Σ ST Δ , mV	1.5 \pm 1.0	1.2 \pm 0.9	1.7 \pm 1.2	1.5 \pm 0.9	NS
- Anterior MI	1.8 \pm 1.1	2.1 \pm 1.0	1.8 \pm 1.3	1.8 \pm 1.0	
- Inferior MI	1.1 \pm 0.7	1.0 \pm 0.7	1.3 \pm 0.1	1.1 \pm 0.6	
In-hospital mortality, %	10	0	19	17	NS

resolution group, but was of similar prevalence to the no resolution group. A trend of lower in-hospital mortality was observed among patients with complete resolution ($p=0.089$).

Variables associated with complete resolution by univariate analysis were inferior infarction ($p=0.00008$), smoking history ($p=0.007$), symptom-onset to treatment time ≤ 4 hours ($p=0.017$), and absence of acute congestive heart failure ($p=0.049$). By multivariate analysis, inferior MI (odds ratio 7.8, 95% confidence interval 2.59-23.68; $p=0.0003$) and smoking history (odds ratio 5.2, 95% confidence interval 1.42-19.07; $p=0.0147$) were independent predictors of complete resolution.

For a subgroup of patients ($n=43$) with interpretable ECGs 60 and 90 minutes after commencement of streptokinase, the incidence of complete resolution increased from 12% at 60 minutes to 26% at 90 minutes ($p=0.01145$). The incidence of partial resolution also increased from 23% to 44%. Conversely, during the same time interval the incidence of no resolution decreased from 65% to 30%. (Figure 1)

Discussion

To our knowledge this is the first analysis on myocardial reperfusion measured by ST resolution at 60 minutes in an Asian population treated with streptokinase for acute myocardial infarction. The ISAM and INJECT substudies reported on ST resolution at 180 minutes after streptokinase in Caucasian patients.^{9,16} Complete ST resolution occurred in about half the patients 180 minutes after streptokinase initiation. Compared with these two studies and recent trials on reperfusion therapy in acute myocardial infarction,^{15,17-18} our population was older, had more diabetes, anterior myocardial infarction, and higher Killip classes. These characteristics are more typical of patients treated in the community rather than those selected for reperfusion trials. Streptokinase was able to restore myocardial perfusion in about a quarter of this high-risk cohort with acute myocardial infarction within 60 minutes of therapy. The unfavourable profile of our population may partly account for the large difference in complete ST resolution measured at an earlier time frame. Our data

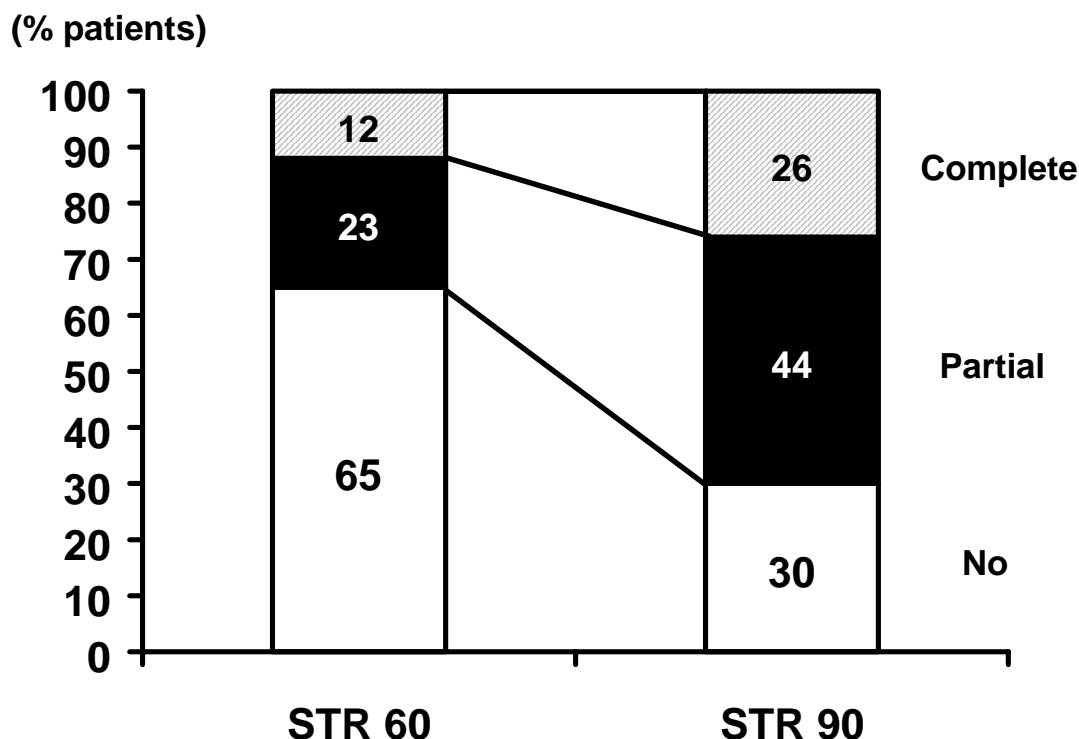


Figure 1. Distribution of ST resolution of 43 patients at 60 and 90 minutes after administration of streptokinase. STR 60=ST resolution at 60 minutes. STR 90=ST resolution at 90 minutes.

also suggested that streptokinase is inferior to lanoteplase, a third-generation fibrinolytic, in accomplishing early myocardial reperfusion. ST resolution at 60 minutes was achieved in 33% of the patients treated with lanoteplase,¹⁹ compared with 24% in our study.

Smoking history (including both current and ex-smokers) and inferior myocardial infarction were identified as independent predictors of successful myocardial reperfusion. These two variables have also been reported as determinants of a lower short-term mortality among patients treated with fibrinolytic therapy in the GUSTO-I trial.²⁰ It has been suggested that smokers have a smaller atherosclerotic burden and a higher thrombus load at the site of coronary occlusion, and therefore respond better to fibrinolytic therapy.²¹ However, subsequent angiographic studies did not confirm this hypothesis. Grines et al²² found that smokers had a larger minimum luminal diameter of the IRA stenosis but a similar percent diameter stenosis whereas Zahger et al.²³ observed no differences with respect to residual stenosis and thrombus grade between smokers and non-smokers. One finding in common is the higher incidence of Thrombolysis in Myocardial Infarction grade 3 flow at 90 minutes, which is the most important factor to account for the short-term survival benefit of smokers. Purcell et al, using the ST resolution in the lead with maximum ST elevation, showed a similar incidence of 50% resolution at 60 minutes between current smokers and non-smokers (44% vs 43%). More non-smokers compared with current smokers failed to achieve a 25% ST resolution by 180 minutes (35% vs 16%).²⁴ Our findings confirm the better response of patients with a smoking history to fibrinolytic therapy and provide additional insight by showing enhanced early myocardial reperfusion in these patients. By mechanisms still unknown, the favourable response to fibrinolysis in current and ex-smokers is seen in the better myocardial reperfusion and is translated into a short-term survival benefit.

We observed in the present study that fewer patients with anterior myocardial infarction achieved complete resolution, a finding consistent with the results of other studies.^{9,16,25-28} This may be explained by the systematic under-estimation of the degree of ST resolution in patients with anterior myocardial infarction because the J point is not uncommonly elevated in the

anterior precordial leads in normal and pathological states.²⁵ Another explanation may be that anterior myocardial infarction is associated with a higher resistance to myocardial reperfusion. A large area of myocardium at risk is present in anterior myocardial infarction. Moreover, more patients with anterior myocardial infarction in the present study had an ischaemic time longer than 4 hours compared with patients with inferior myocardial infarction (36% vs 17%, $p=0.037$). Both factors are related to oxidative stress and a lack of recovery of aerobic metabolism. Subsequent neutrophil plugging of capillaries and oedema lead to an increased impedance to flow.^{11,19} These factors may account for the poor response of anterior myocardial infarction to fibrinolytic therapy for myocardial reperfusion compared with inferior myocardial infarction.

The prognostic value of 60-minute ST resolution has been validated in the InTIME-II substudy. A stepwise correlation exists between 60-minute ST resolution and both the short- and long-term mortality.¹⁹ In the present study, we also noted a trend for lower in-hospital mortality among patients with complete resolution. Although a proportion of patients developed complete resolution without further treatment from 60 to 90 minutes, approximately three-quarters of the patients still did not achieve complete resolution by 90 minutes after initiation of streptokinase. By analysing the ECG 60 minutes after fibrinolytic therapy, a simple, quick, and non-invasive method is available to guide decision on further management. For patients without complete ST resolution by 60 minutes, a large proportion (84%) will continue to have partial or no resolution by 90 minutes. These patients either have the infarct-related artery persistently occluded, or no myocardial salvage despite a patent infarct-related artery by angiography.^{8,25} Given the promising results of rescue percutaneous transluminal coronary angioplasty, this group of patients should be considered for emergency revascularisation.

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