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Acute Anterior Myocardial Infarction: Streptokinase Prevents Ventricular Thrombosis Independently of Its Effect on Infarct Size

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Summary: Left ventricular thrombosis (LVT) is a frequent complication after acute anterior myocardial infarction (AMI). The purpose of this study is to evaluate whether streptokinase (SK) therapy prevents LVT, and whether this effect is due to the preservation of left ventricular function or to the fibrinolytic action of the drug. Sixty-five patients who underwent a left ventricular angiography within 2 months after a first AMI were studied. Twenty-eight patients (SK group) received SK 1,500,000 U i.v. administered over 60 min within 6 h from the onset of symptoms. A lower incidence of LVT was found in the SK group ($p=0.0003$). We divided patients into two classes according to the value of akinetic-dyskinetic area (AD): the first group with a lower value of AD, the second group with a higher value of AD. In both groups, a reduced incidence of LVT was associated with SK therapy ($p=0.014$, $p=0.015$, respectively). Early infusion of SK during AMI seems to prevent the development of LVT, with an effect partly independent from its action on infarct size for small to large myocardial infarction.

Key words: myocardial infarction, streptokinase, left ventricular thrombosis

Introduction

The formation of a left ventricular thrombus (LVT) is a fairly frequent complication of acute anterior myocardial infarction (AMI). An incidence of 36% has been reported[1-4] by echocardiography versus an incidence of 46% found by Lamas *et al.*[3] with left ventriculography. While LVT has not been a frequent finding in non-Q and inferior infarction, it often occurs in anterior, anterolateral, and apical acute myocardial infarction, presumably as a consequence of the greater extent of infarct size.

There is evidence that the formation of thrombus occurs early after the appearance of AMI symptoms.[2,5] The major factors involved in this process are stasis, endocardial necrosis, and thrombophilic tendency. The use of fibrinolytic therapy with streptokinase (SK) in the early stages of an AMI has introduced a new variable in the evolution of this disease and its complications.

The purpose of this study is to assess whether LVT is reduced by the use of SK and whether prevention of LVT is due to a direct effect of fibrinolytic therapy on thrombus formation or to an indirect effect through preservation of the ventricular function.

Materials and Methods

The patient population consisted of 65 consecutive patients, 55 males and 10 females, mean age 54.6 ± 8.7 years, who underwent left ventricular angiography between July 1985 and December 1989, following acute anterior myocardial infarction.

Cardiac catheterization was performed within two months after myocardial infarction (mean 23.2 ± 10.3 days) in relation to postinfarction angina, heart failure, or severe arrhythmias. Concomitant treatment with heparin was investigated. Left ventricular angiography was performed during cardiac catheterization using 8-F pigtail Cordis (femoral approach) or NIH Cordis (brachial approach) catheters. A total of 40 ml of radiographic contrast was injected at 20 ml/s near the left ventricular apex. Left ventricular end-diastolic pressure was measured before ventriculography.

LVT was determined as a contrast defect in the opacification of the left ventricle, unrelated to the anatomic structure of the cavity (Fig. 1). Left ventricular volumes (end-

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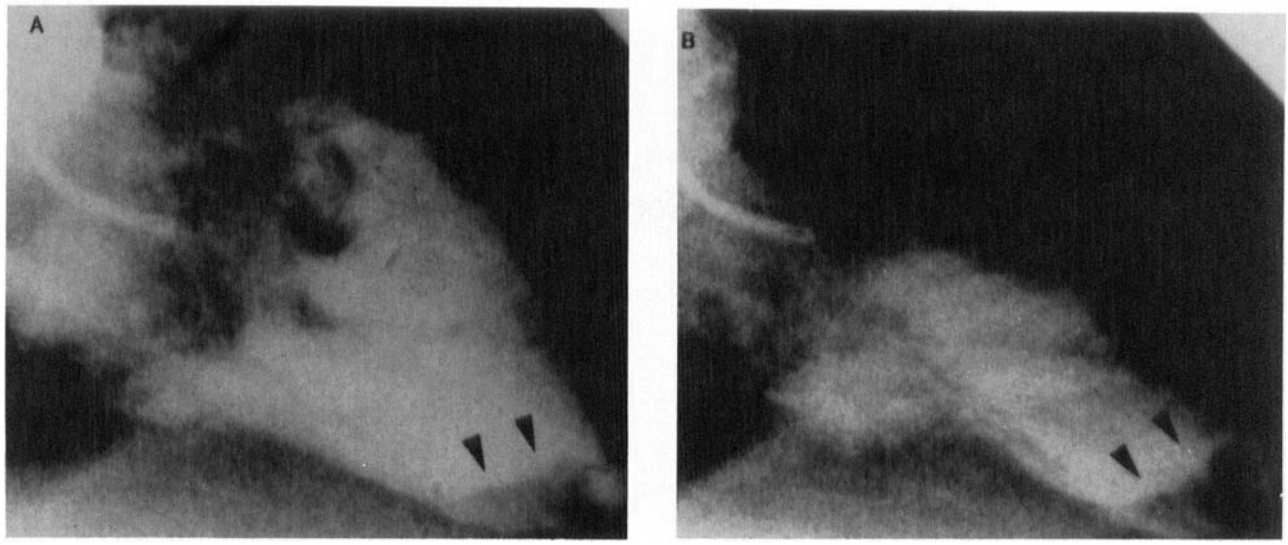

FIG. 1 Cineangiogram in diastole (A) and systole (B), of a patient with mural left ventricular thrombus (arrow).

diastolic and end-systolic) and ejection fraction were measured using the method of Dodge[6] for a single plane in the right anterior oblique projection at 30 degrees. Left ventricular kinetics were determined by superimposing the diastolic and systolic silhouette area.

A segment was defined as akinetic when a total absence of wall motion was observed and as dyskinetic when a paradoxical systolic expansion was observed. Planimetry of the akinetic-dyskinetic area was performed. The extension of akinetic-dyskinetic area (AD) was expressed as a percentage of the total diastolic area (Fig. 2).

Statistical Methods

Data are expressed as mean ± 1 SD. Differences between means were assessed using Student's *t*-test for unpaired data. Categorical data were analyzed by Chi-square test or Fisher exact test, as appropriate. A two-tailed p value less than 0.05 was considered to be statistically significant.

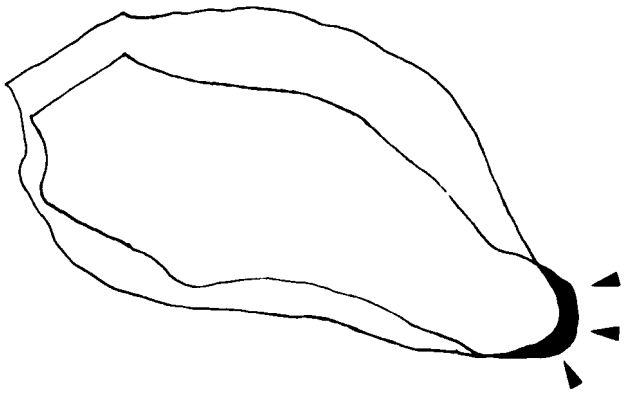

FIG. 2 Right anterior oblique silhouette of the left ventricle used to calculate volumes and akinetic-dyskinetic area (arrow).

Results

Out of 65 patients, 28 (43%) were treated by streptokinase therapy (SK group); 37 patients (57%) did not receive thrombolytic therapy (control group).

The hemodynamic parameters evaluated were not statistically different between the SK group and control group, although a slight trend toward better function of the left ventricle in the SK group was present (Table I).

LVT was found in 23 (35.4%) of 65 patients, 3 in SK group (13%), and 20 in the control group (87%). In 42 patients, no left ventricular thrombosis was evident: 25 (59.5%) were SK patients and 17 (40.5%) were in the control group. The difference is highly statistically significant ($p=0.0003$).

The percentage of patients on heparin therapy did not differ significantly between patients with or without LVT ($p=0.22$).

The hemodynamic-angiographic parameters gave evidence of more compromised left ventricular function in patients with LVT (Table II), with a significantly higher AD.

In order to evaluate the influence of thrombolytic therapy on the formation of LVT, independent of its effect on left ventricular function, we divided the patients into two groups according to the average value of AD distribution (16.8%) computed for all patients. We obtained one group with a smaller AD ($\leq 16.8\%$) and a second group with a larger AD ($>16.8\%$). In both groups, patients treated with SK had a statistically significant lower incidence of LVT (Table III).

TABLE I Parameters of left ventricular function in 28 patients treated with streptokinase (SK) versus the 37 control patients (C)

	SK	C	p Value
Patients (n=65)	28	37	
AD (%)	15.10±14.93	18.10±17.03	.45
EDVI (ml/m²)	94.96±25.74	103.05±33.48	.27
ESVI (ml/m²)	56.21±25.62	64.91±34.48	.24
EF (%)	42.10±13.37	39.16±14.88	.40
EDP (mmHg)	17.53±8.13	18.56±9.73	.64

Abbreviations: AD=akinetic-dyskinetic area; EDVI=end-diastolic volume index; ESVI=end-systolic volume index; EF=ejection fraction; EDP=end-diastolic pressure.

TABLE II Parameters of left ventricular function in patients with (+LVT) and without (−LVT) left ventricular thrombus

	+LVT	−LVT	p Value
Patients (n=65)	23	42	
AD (%)	25.39±16.39	9.51±12.72	.0002
EDVI (ml/m²)	114.47±30.67	86.17±26.76	.0005
ESVI (ml/m²)	79.08±30.92	45.58±24.96	<.00001
EF (%)	31.08±12.07	48.26±12.58	<.00001
EDP (mmHg)	21.39±9.75	15.34±7.81	.01
SK	3 (13%)	25 (59%)	.0003

See Table I for abbreviations.

TABLE III SK therapy and left ventricular thrombosis (LVT) in smaller (AD≤16.8%) and large (AD>16.8%) infarctions

	+LVT	−LVT	p Value
AD≤16.8%: SK (n=38)	1 (2.6%)	17 (44.7%)	.014
AD>16.8%: SK (n=27)	2 (7.4%)	8 (29.6%)	.015

Discussion

The Role of Myocardial Necrosis on the Development of LVT

Johnson *et al.*[7] have shown striking alterations in the endocardium lining of the infarcted area in the first 24 h after acute myocardial infarction. The alterations include endothelial desquamation, revealing a denudated subendothelial surface, and concomitant leukocytic invasion of the endocardium. The basal lamina, which is perforated in several places, exposes collagen fibrils. Collagen may activate the aggregation of platelets, commencing the process of thrombus formation, although no definite conclusions have been drawn.[8,9]

Two-dimensional echocardiographic observation of LVT of the infarcted area 36 h after the onset of symptoms[5] could reinforce this theory.

The Role of SK

Local effect. SK forms a stochiometric complex with plasminogen. The complex has proteolytic activity and converts circulating and thrombus-bound plasminogen to plasmin.[10] α_2-Antiplasmin rapidly inactivates the circulating plasmin, but not the thrombus-bound plasmin which is protected from antiplasmin. Consequently early administration of SK during AMI could have a lytic effect on developing ventricular thrombosis, as previously reported by Kremer *et al.*[11] The use of urokinase 60,000 U/h for 2–8 days has been proved effective to dissolve LVT in the first month of an AMI. The presence of a severe compromised ejection fraction reduced the efficacy of the thrombolytic therapy. Due to its similar thrombolytic activity, SK should have a comparable effect.

Systemic effect. The systemic fibrinogenolytic effect is very important,[12] if we consider that a higher circulating

fibrinogen peak has been recorded on the fourth day of AMI in patients with LVT not treated with SK.[13] The same data have been reported in patients with systemic or pulmonary embolization during AMI.[14] α_2-Antiplasmin is able to inactivate about 60% of circulating plasmin, but is rapidly exhausted by the increased amount of plasmin produced by high doses of SK. As a result, systemic fibrinogenolysis occurs. The administration of more than 500,000 U of SK exhaust the circulating plasminogen supply and deplete 90% of the fibrinogen. Moriarty *et al.*[15] report a reduction in plasma fibrinogen concentration 1 h after SK infusion of 600,000–1,500,000 U over 30 min, which lasts for 36–48 h. The plasma fibrinogen reduction acts on red cell aggregation, causing a reduction in whole blood viscosity, which remains depressed for 6 days. Concomitant with reduced fibrinogen, there is an increase of fibrinogen degradation products. Levels of fibrinogen degradation products remain elevated for 24–48 h and have anticoagulant properties due to inhibition of platelet aggregation and fibrin polymerization. These data illustrate the complex activity of SK. In response to the initial direct thrombolytic effect, an anticoagulant action lasting 24–48 days follows. As a consequence, the formation of LVT is less frequent in the first two days after SK therapy. We could not measure any parameter of thrombolytic activity of SK because of the retrospective protocol of the study; however, we had used comparable doses of SK (1,500,000 U in 60 min), and thus a similar effect on blood coagulation and viscosity could reasonably be expected.

The Role of Infarct Size on the Development of LVT

Endocardial injury and stasis of blood during AMI can justify the development of thrombus, mainly on an akinetic or dyskinetic apex, where blood exchange is reduced over the cardiac cycle.[3,16] The more compromised ventricular function among patients with LVT confirms previous data.[3]

Some authors[17–19] report significant improvement in left ventricular function with SK treatment; our results, however, in accordance with those of other authors,[20] show that left ventricular function in the SK group was not significantly improved, even though a trend toward better ventricular function in thrombolysed patients was present. This could be because patients who underwent coronary and left ventricular angiography were mainly those with complicated AMI (heart failure, angina, arrhythmias). SK, however, significantly reduced left ventricular thrombus formation in our patients, both in the group with a smaller AD and the group with a larger AD; the effect seems to be partially independent of the direct effect on left ventricular function. Held *et al.*[21] reported a similar trend in their SK group, but the difference was not statistically significant; the number of patients with LVT was smaller and, moreover, a subgroup of patients was treated with tissue-type plasminogen activator and did not exhibit a reduction of LVT incidence.

Conclusion

Our data seem to suggest that early infusion of SK (within 6 h from the onset of symptoms) can prevent the development of LVT, for small ($AD \leq 16.8\%$) to large ($AD > 16.8\%$) acute myocardial infarction. The SK activity appears to be partially independent of its effect on infarct size and probably is the result of local and systemic fibrinolysis.

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