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Early Cardiac Rupture Following Streptokinase in Patients with Acute Myocardial Infarction: Retrospective Cohort Study

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Aim. To assess the incidence and timing of cardiac rupture following streptokinase (SK) administration in acute myocardial infarction (AMI).

Methods. We retrospectively analyzed the clinical sheets of AMI patients treated at the Coronary Care Unit in University Hospital Split, Croatia, between January 1, 1996, and December 31, 1998. We selected the patients who died following SK administration (1.5 million U in a 30 min iv. infusion), with a discharge diagnosis of "AMI" and "cardiac tamponade – ventricular rupture". AMI was defined by typical chest pain, ECG, and/or enzymatic changes. Echo or autopsy verified diagnosis of cardiac tamponade and/or rupture, as well as pericardial effusion and/or free-wall rupture.

Results. Out of 726 AMI patients 136 (18.7%) were treated with SK, and 6 had cardiac rupture (4 men and 2 women; 4.4%). Autopsy revealed that 1 patient had ischemic and 2 had transmural hemorrhagic AMI. Three out of 6 patients died 2-4, and 3 died 5-7 hours after SK administration. Six patients who died from cardiac rupture (mean age 72.3±9.0) were significantly older than AMI survivors treated with SK (121 patients, mean age 60.5±12.0 years, $p<0.001$).

Conclusion. In case of unexplained clinical deterioration in AMI patients over 70 during the first hours after SK administration, cardiac tamponade due to a free-wall rupture should be suspected. SK administration in patients with AMI over 70 years should be a selective and not a routine treatment.

Key words: *cardiac tamponade; heart rupture, post-infarction; ischemic heart disease; ischemia, myocardial; myocardial infarction; streptokinase*

Cardiac rupture is a catastrophic complication that occurs between 4 and 6 days in 3% to 4% of the patients with acute myocardial infarction (1). Free-wall rupture occurs only after acute transmural necrosis (1).

Although many large controlled trials demonstrated that thrombolysis, performed during the first few hours after acute myocardial infarction symptoms, decreases the infarct size, improves left ventricular function, and reduces the death rate by some 50%, caveats regarding the side effects of thrombolysis are advanced (1-3).

Beside various allergic reactions and/or visceral hemorrhage (especially cerebral and pericardial), cardiac rupture is a major risk of streptokinase treatment in acute myocardial infarction and has been found in almost 38% of autopsies in clinical trials of thrombolytic agents (2-4). According to the literature's data and our own clinical experience, free-wall cardiac rupture is a relatively common and sometimes very early complication of streptokinase therapy in patients with acute myocardial infarction.

The aim of this study was to assess the incidence and timing of cardiac rupture following streptokinase administration in patients with acute myocardial infarction.

Methods

We retrospectively analyzed the clinical sheets of patients with acute myocardial infarction, treated in the Coronary Care Unit, Department of Internal Medicine, Split University Hospital, between January 1, 1996, and December 31, 1998. We selected the patients who died after streptokinase administration with a discharge diagnosis of "acute myocardial infarction" and "cardiac tamponade – ventricular rupture". Acute myocardial infarction was defined as prolonged

(>30 minutes) typical chest pain not responding to nitroglycerin, with sustained ST-segment elevation and/or appearance of new Q-waves and/or duplication of the creatine-phosphokinase normal values. Clinical suspicion of cardiac tamponade and/or rupture was echocardiographically verified by pericardial effusion and free-wall rupture or, at autopsy, by acute myocardial infarction with hemopericardium and ventricular wall rupture.

Results

There were 726 patients with acute myocardial infarction during the studied period. Out of 726 patients with acute myocardial infarction, 136 (18.7%) were treated with streptokinase (1.5 million U, in 30 min as an iv. infusion). There were 89 (65.4%) men, age 59±13 years, and 47 (34.6%) women, age 64±11 years. Fifteen out of 136 patients with acute myocardial infarction (9.0%) treated with streptokinase ("streptokinase group") died. In contrast to that, in "no streptokinase group" mortality was significantly higher (110 out of 590 patients died, 18.6%; $p<0.001$; odds ratio 3.3). There were 6 patients, 4 men and 2 women (6/136 or 4.4%), with the discharge diagnosis of acute myocardial infarction and cardiac rupture confirmed by either echocardiography (6/6) or at necropsy (3/6). Three deceased patients did not undergo autopsy. The necropsy revealed that one patient had ischemic and two had transmural hemorrhagic acute myocardial infarction. Six patients died in a cardiogenic shock, 4 of them had electromechanical dissociation, and 3 died in ventricular fibrillation after unsuccessful reanimation. In the "no streptokinase group", during in-hospital phase of acute myocardial infarction, 10 out of 590 (or 1.7%) patients died under the clinical suspicion on cardiac tamponade. In 2 of them, free-wall rupture was verified at necropsy.

Clinical data of 15 patients with acute myocardial infarction who died following streptokinase were compared to 121 patients who survived streptokinase treatment (Table 1). Three out of 6 patients who died due to ventricular free-wall cardiac rupture, died between 2 and 4 hours, and 3 of them died between 5 and 7 hours after the start of streptokinase administration.

Table 1. Clinical data on patients with acute myocardial infarction (AMI) treated with streptokinase according to the patients' survival

Variable	AMI death due to		AMI[b] survivors
	cardiac rupture	other reasons	
No. of patients	6	9	121
Age (years)[b]	72±9[a]	65±11	61±12[a]
Anterior AMI (No.)	4	4	62
Inferior AMI (No.)	2	5	59
"Pain to needle" time (h)[c]	4 (1-7)	5 (1-10)	6 (3-9)
"Needle to rupture-death" time (h)[c]	8.5 (2-20)	1 h-10 days	–

[a]$p<0.001$.
[b]Mean±SD.
[c]Median (range).

Discussion

Caridac rupture, a catastrophic streptokinase side effect, occurs only in the presence of acute transmural myocardial necrosis (1). Thrombolytic therapy promotes hemorrhage into the fresh infarction area, whereas cardiac rupture is often caused by blood dissection through regions of transmural necrosis (5). Although collagen plays a specific role in the maintenance of vascular integrity and in the thrombosis and scar formation, increased collagen degradation followed by inhibition of collagen synthesis in the infarcted myocardium might increase the risk for cardiac rupture, especially after streptokinase treatment (6).

Although there are some reports that early thrombolytic therapy improves survival and decreases the risk of free-wall rupture, and late administration also improves survival but increases the risk of cardiac rupture (7), we did not find such a difference. Most authors agree that older age (over 65 or 70 years) increases the risk of cardiac or septal wall rupture and of hemopericardium following streptokinase in the treatment of acute myocardial infarction (3,4,7,8). Some have reported early hemorrhagic pericardial effusion without ventricular free-wall rupture in patients with large anterior myocardial infarction, treated with thrombolytics within 4 hours of the onset of symptoms (8). Transthoracic echocardiography seems to be the screening method of choice in the early diagnosis of cardiac tamponade, cardiac rupture, and pericardial effusion (9). Evidence of early cardiac rupture in our patients with acute myocardial infarction (within 2 to 4 hours, a very short "needle-to-rupture time" not reported in the literature!), might be explained by increased collagen degradation in older patients (over 70 years), who probably have increased collagen content in the heart and vessels (6). This early free-wall rupture (within the first 24 hours) in the patients with acute myocardial infarction should be promoted by slit-like tear which develops between the viable (contractile) and the dead (non contractile) myocardium (10).

In-hospital, free-wall cardiac rupture observed in this cohort of patients (4.4%) was comparable to similar studies (varying between 1.4% and 4.8%) (8,9,11). Such relatively common side effect of streptokinase treatment in patients with acute myocardial infarction could be probably decreased by urgent pericardiocentesis and by surgical repair (11). Some authors report decreased mortality in patients with acute myocardial infarction following streptokinase, mainly due to reduced rate of cardiac rupture (12).

All our patients with cardiac rupture, as in other studies (12), had sudden electromechanical dissociation. This finding strongly supports the correlation between left ventricular free-wall rup-

ture and electromechanical dissociation. We might suggest that some of our patients who died due to other causes following streptokinase administration, and developed electromechanical dissociation, probably had cardiac tamponade.

In conclusion, we believe that, in the presence of unexplained clinical and hemodynamic deterioration, with electromechanical dissociation, in patients with acute myocardial infarction over 70 years during the first few hours after streptokinase administration, cardiac tamponade due to free-wall rupture should be suspected, and easily confirmed by transthoracic echocardiography. We recommend a not routinely but a carefully and individually reconsidered streptokinase use in patients over 70 years of age with acute myocardial infarction.

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