P3653 Lytic activity profile of 1.5 MU streptokinase infused in 60 minutes for acute myocardial infarction

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The two mechanisms limiting the efficiency of the thrombolytic activity of streptokinase (SK) are the neutralization with specific antibodies or inhibitors and the plasminogen depletion with subsequent plasminogen-steal effect resulting from the formation of the activator (SK-plasminogen complexes). The current dose of 1.5 MU SK given in 60 minutes (min) was designed to overcome the first factor, without taking consideration to the second factor. To explore this, the net lytic activity (L Act) of this regimen was investigated by ex vivo measurement of lysis onset time (LOT) of fresh autologous thrombus using a bedside thrombolytic assessment system (TAS; Cardiovascular Diagnostic System, Inc.) before 10, 20, 60 and 180 min after start of SK infusion in 58 AMI pts. L Act is proportionate to shortening of LOT and is non-detectable when LOT >1200 seconds (sec). Lytic Reserve assessed by the LOT response to 1,000 U/ml t-PA in vitro (normally <300 sec) was determined at baseline and after 180 min.

Results: LOT determinations are expressed as median.

	Baseline	10 min	20 min	60 min	180 min
LOT (sec)	>1200	173*	242**	802*	1022
% Pts LOT >1200	100	12	17	34	46°
% Pts LOT <300	0	71	62	26	27°°
LOT (sec) in vitro t-PA	106	–	–	–	>300*
% Pts with Lytic Reserve	100	–	–	–	6*

* $p < 0.001$; ** $p < 0.02$ vs preceding results. ° $p = 0.0005$; °° $p < 0.0001$ for sequential changes.

Conclusions: 1) Rate of initial resistance to SK was found to be 12% most likely due to neutralization effect. 2) L Act was inversely related to the cumulated infused dose of SK, with an important impact beyond 20 min (500,000 U). 3) 1.5 MU SK exhausted the Lytic Reserve. Plasminogen-steal effect appears therefore to represent the dominant limiting factor of efficient L act.

P3654 Comparison of lytic activities during accelerated t-PA and streptokinase infusion in patients treated for acute myocardial infarction

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Based on early infarct-related coronary patency and mortality, accelerated t-PA was established superior to the 60-min infusion of 1.5 MU of streptokinase (SK) in acute myocardial infarction (AMI) (Gusto 1). Although the fibrin specificity may explain in part the better efficacy of t-PA, it has not been demonstrated at the level of lysis activation. Accordingly, to compare lytic activities of two different thrombolytic agents, lysis onset time (LOT) of a fresh autologous thrombus was determined ex-vivo using a bedside thrombolytic assessment test (TAS; Cardiovascular Diagnostics Inc., USA) at baseline, 10 min after bolus, end of infusion, 180 min, in 58 pts with AMI treated with 1.5 MU SK and 61 pts with accelerated t-PA. Lytic activity (L Act) is inversely proportional to LOT.

Results: After t-PA bolus, LOT decreased <300 sec in 98% of pts and after SK in 71% ($p = 0.002$). Using the threshold of LOT <300 sec as the one observed in 98% of pts given t-PA, the L Act during infusion remained more efficient with t-PA than with SK. By contrast, at 180 min, efficient L Act is still present in more pts treated with SK.

% of pts with LOT <300 sec

	Baseline	10 min	20 min	End Infusion	180 min
t-PA	0%	98%	–	88%	3%
SK	0%	71%	62%	26%**	28%*

* $p = 0.002$; ** $p < 0.001$ versus t-PA

Conclusions: 1) unlike previous hematologic assays, this new method of assessment of L Act provides a direct evidence of the biological superiority of t-PA over SK related to the higher infarct-related coronary patency rate, achieved at 90 min with t-PA; 2) sustained L Act beyond 90 min observed with SK is consistent with a lower rate of early reocclusion.

P3655 Smoker's paradox in acute myocardial infarction: no relation to higher patency rates after intravenous thrombolysis, primary PTCA or spontaneous reperfusion

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It has been suggested that compared to nonsmokers (NSM), smokers (SM) with acute myocardial infarction (AMI) have a more favorable prognosis, and that this "smoker's paradox" may be related to a larger contribution of thrombosis to acute coronary occlusion. Therefore, SM may have less extensive coronary artery disease, and superior sensitivity to reperfusion interventions.

To investigate this issue, we examined 790 consecutive patients (pts) admitted ≤6 hours after onset of AMI. Of these pts, 555 (70%) were SM, and 235 (30%) NSM. Acute angiography was performed in all pts, after either intravenous thrombolysis (with standby rescue PTCA), primary PTCA, or suspected spontaneous reperfusion.

	Smokers	Nonsmokers	p
Age (years)	56	67	$<10^{-5}$
Male	502 (91%)	142 (60%)	<0.01
Multivessel disease	236 (42%)	113 (48%)	NS
Cardiogenic shock	18 (3%)	18 (8%)	<0.01
Spontaneous reperfusion	42 (8%)	19 (8%)	NS
Thrombolysis			
– Attempted	258 (46%)	7 6 (32%)	<0.001
– Success, pre-Rescue PTCA	169 (66%)	50 (66%)	NS
– Success, post-Rescue PTCA	235 (91%)	64 (84%)	NS
Primary PTCA			
– Attempted	243 (44%)	125 (53%)	<0.02
– Success	226 (93%)	120 (96%)	NS
Reperfusion, overall	503 (91%)	203 (86%)	NS
In-hospital mortality	26 (5%)	37 (16%)	$<10^{-5}$

Conclusions: Since there is no difference between groups in terms of spontaneous, post-thrombolysis or post-PTCA patency rates during AMI, the higher mortality observed in NSM compared to SM appears mainly related to worse baseline characteristics.

P3656 After thrombolytic therapy smokers with complex culprit lesions have lower reocclusion rates than non-smokers

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In the APRICOT-study the primary endpoint was reocclusion of culprit coronary lesions at 3 months after successful thrombolysis. In this study a total of 248 patients (pts) underwent coronary angiography within 48 hours after successful thrombolysis and after 3 months. The morphology of the culprit lesion at the first angiography was prespecified as smooth or complex. Changes in morphology and severity were related to baseline clinical and demographic characteristics.

Results: Among the 108 pts with complex culprit lesions 61 pts smoked and 47 did not. Of the 61 smokers 9 (15%) had reocclusion. Of the 47 non-smokers 15 (32%) had reocclusion ($p < 0.05$). Of the 84 pts with complex lesions without reocclusion 51 were smoker and 33 were not. Of the 51 smokers 28 (74%) showed a favourable change to smooth morphology with a concomitant reduction in severity. Of the 33 non-smokers this change occurred in 10 pts (26%) ($p < 0.05$). These differences were not seen in pts with smooth culprit lesions.

In conclusion, after thrombolysis for acute myocardial infarction smoking is associated with a favourable remodelling of complex culprit lesions with a concomitant reduction in severity and a lower reocclusion rate. Possibly, the hypercoagulable state that has been shown to exist in smokers, accounts for a larger thrombotic component in complex lesions seen after thrombolysis. These lesions are more subject to ongoing thrombus resolution.