In contrast, in the MS group there was no additional decrease in ST shift during the second and third inflation compared with the first. The reduction in ST shift afforded by MS during the first inflation (−51% on IC-ECG vs first inflation in C) was equivalent to that afforded by ischemic preconditioning in controls (−44% during the third vs first inflation). In conclusion, pretreatment with MS mimics ischemic preconditioning during PTCA. To our knowledge, these results provide the first evidence that morphine preconditions human myocardium against ischemia in vivo and suggest that opioid receptors may play a role in the signaling pathways responsible for ischemic preconditioning in man. Because of its efficacy and safety, morphine could be used prophylactically to attenuate ischemia in high risk PTCA.

11:15

810-4 Brief Antecedent "preconditioning" Ischemia Accelerates Coronary Thrombolysis in the Canine Model

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Background: It is well-established that brief episodes of antecedent ischemia "preconditon" (PC) the heart and reduce infarct size caused by subsequent sustained coronary occlusion. In addition, recent studies from our laboratory revealed that brief antecedent PC ischemia also attenuates subsequent platelet aggregation in damaged and stenotic coronary arteries by an adenosine-mediated mechanism. Our current aim was to determine whether the antiplatelet properties of PC ischemia result in more rapid reperfusion and better maintenance of subsequent vessel patency in the setting of coronary thrombosis/thrombolysis.

Methods: Anesthetized dogs underwent 10 min PC ischemia + 10 min reflow (n = 7) or no intervention (n = 7) prior to initiation of thrombotic coronary artery occlusion. At 1 h after the onset of thrombosis, all dogs received 1.3 mg/kg rt-PA. Primary study endpoints included the time required to achieve reflow; the duration of spontaneous reocclusion during the 2 h after initial lysis; and the total duration of thrombotic occlusion (all with nonparametric distributions and thus reported as the median [25th; 75th] percentiles). As secondary endpoints, collateral blood flow was measured during thrombotic occlusion by injection of radiolabeled microspheres, and infarct size delineated by tetrazolium staining and expressed as a % of the myocardium at risk.

Results:

	Control	Preconditioned
Time to lysis (min)	47 [13; 50]	11 [7; 14]**
Time spent reoccluded (min)	20 [2; 52]	6 [0; 10]
Total time occluded (h)	1.9 [1.6; 2.6]	1.3 [1.1; 1.4]**

The time required to achieve initial lysis was significantly shortened, and subsequent vessel patency tended to be better maintained, in dogs that received antecedent PC ischemia vs controls (**p < 0.05). This was, not surprisingly, accompanied by a significant reduction in infarct size (11% vs 32% of the risk region; p < 0.05), despite comparable collateral perfusion, in the PC group.

Conclusions: Brief preconditioning ischemia – in addition to its well-documented cardioprotective properties – markedly shortens the time required for rt-PA-induced thrombolysis in this canine model.

11:30

810-5 In Vivo Suppression of Myocardial Apoptotic Cell Death by Insulin-like Growth Factor IGF I and II

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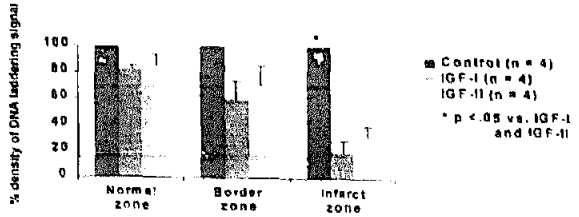
Background: Apoptosis (Apo) is a form of programmed cell death occurring in physiological and patophysiological states including myocardial infarction (MI). Insulin-like growth factors (IGF) I and II have been shown to suppress Apo in vitro, but their in vivo effects are unknown. The purpose of this study was to examine the effects of intracoronary IGF-I and II administration on myocardial Apo in acute MI.

Methods: Coronary microembolization was performed using 100μ affigel beads in pigs randomly assigned to 0.5 μg IGF-I, IGF-II, or bovine albumin, incorporated within the beads and gradually released. After sacrifice at 4 weeks, myocardial samples from the infarct (I), border (B), and normal zones (N) were assessed for Apo by TUNEL and ligation-mediated PCR.

Results: TUNEL-positive cells were observed particularly in I and B and were reduced in the treated animals. Using PCR, IGF-I and II were also found to reduce the DNA laddering signal in I, with a similar trend in B (see figure).

Conclusions: Both IGF-I and II suppressed Apo in this porcine model of acute myocardial infarction, supporting a role for IGF-I and -II in regulating myocardial Apo in vivo.



11:45

810-6 Use of a Novel Anti-Apoptotic Agent (LXR017) Reduces Infarct Size Following Ischemia-Reperfusion in the Canine Myocardium

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We have previously shown that a phospholipid agent (LXR017) specifically prevents apoptotic cell death induced by serum/glucose deprivation, a parallel to in-vivo ischemia reperfusion injury, in rat neonatal cardiomyocytes. Since apoptosis plays a major role in myocardial cell death following ischemia reperfusion, we sought to test the efficacy of LXR017 in an in-vivo model of ischemia reperfusion. Twenty open-chested dogs underwent temporary LAD occlusion (90 min) followed by reperfusion (3 hrs). All dogs had continuous monitoring of ECG, left ventricual pressure, and dP/dt. Fifteen min prior reperfusion, dogs were randomly administered either an intracoronary infusion of placebo (n = 6), SOD-Catalase (5 mg/kg; n = 5) a positive control group, or LXR017 (250 μg; n = 9) for a total of 75 min. Endpoints included infarct size measured by TTC staining (% of area at risk), regional shortening fraction (SF) via sonomicrometer crystals, regional myocardial blood flow via radioactive microspheres, and myeloperoxidase (MPO) activity. Baseline hemodynamics as well as regional myocardial blood flow were similar among groups and did not differ during the course of the study. Infarct size, MPO and SF findings at 3 hrs of reperfusion indicate that LXR017 protects the ischemic-reperfused canine myocardium, and may provide a valuable new adjunct to reperfusion therapy for acute myocardial infarction.

	Infarct Size (%)	MPO (U/min/g)	SF (%)
Placebo	22 ± 2	0.198 ± 0.09	3.32 ± 3.08
SOD-Catalse	11 ± 6*	0.096 ± 0.01*	2.82 ± 2.85*
LXR017	10 ± 4*	0.094 ± 0.03*	3.12 ± 2.59*

Data are presented in mean ± SD *P 0.04 vs Placebo by ANOVA

811 Dilated Cardiomyopathies: New Observations and Approaches

Monday, March 30, 1998, 2:00 p.m.–3:30 p.m.
Georgia World Congress Center, Room 367W

2:00

811-1 The Frequency of Familial Disease in a Consecutive Series of 51 Patients With Idiopathic Dilated Cardiomyopathy

A. Gavazzi, M. Ponzetta, C. Campana, M. Giraldi, C. Inserra, A. Raisaro, M.L. Laudisa, E. Colombi, B. Del Bello[1], E. Arbustini[1]. *Divisione di Cardiologia, Italy;* [1]*Istituto di Anatomia Patologica dell'Università, IRCCS Policlinico S. Matteo, Pavia, Italy*

Background: Familial disease may account for a significant proportion of patients with dilated cardiomyopathy (DCM) and could be more frequent than is often recognised. Most previous reports are of anedoctal or retrospective nature and only a few prospective studies have been published. Consequently, the real frequency of familial disease in DCM remains to be established.

Methods: Our aim was to assess the frequency and mode of inheritance of familial disease by prospectively screening relatives from a series of 51 consecutively diagnosed patients with DCM. The diagnosis of DCM was confirmed invasively in every patient. All patients had a 2–3 generation pedigree constructed. Familial disease was diagnosed when at least one relative was affected by DCM. Screening consisted of history, clinical examination with blood pressure measurement, 12 lead ECG, two dimensional Doppler echocardiography, signal averaged ECG (SAECG) and blood sample (serum CK).

MONDAY ORAL