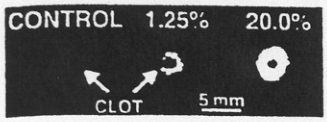
2.5, 5, 10 and 20 mole%. Biotinylated antifibrin monoclonal antibodies (NIB 5F3) and avidin were used to couple the emulsion nanoparticles to fibrin clots. Magnetic resonance imaging of the targeted clots suspended in blood was performed with a Philips Gyroscan ACS-NT (1.5 T) and T1 was calculated using the Look-Locker technique.

Results: Increasing concentrations of Gd-DTPA improved T1 shortening of targeted clots monotonically. T1 relaxation was decreased maximally ($p < 0.05$) at the 20 mole% level (602 ms) vs. control (1218 ms).



Conclusion: Detection of fibrin deposits, particularly microthrombi on the surface of vulnerable atherosclerotic plaques requires high concentrations of gadolinium to provide adequate sensitivity. Fibrin-targeted perfluorocarbon emulsion nanoparticles can provide a stable platform ideally suited to deliver tens of thousands of gadolinium atoms into microscopic fissures in unstable plaques. This novel targeted MRI agent may allow sensitive, early detection of unrecognized vascular pathology in high-risk patients and allow implementation of preventative therapies to reduce associated morbidity and mortality.

1111-44 Serum Glucose but Not Insulin Modulates Platelet-Dependent Thrombosis in Patients With Coronary Artery Disease

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Background: Previously we demonstrated that elevated blood glucose (G) is associated with augmented platelet-dependent thrombosis (PDT). High plasma insulin (I) levels are associated with enhanced risk of CAD, however, the mechanisms are unknown.

Methods: We prospectively measured PDT in 36 stable CAD patients (mean age 68 ± 9 years) on aspirin with controlled lipid levels. Porcine aortic media was exposed to flowing non-anticoagulated venous blood using an ex-vivo perfusion (Badimon) chamber. PDT was measured by computerized morphometry. Total plasma immunoreactive I and G levels were measured after overnight fast.

Results: Initial correlation analysis between I, G and PDT demonstrated I ($r = 0.015$, $p = 0.93$) and G ($r = 0.51$, $p = 0.002$). Patients were divided into two groups: Group A ≤ and Group B > the median I level (17 μU/ml). There were no significant differences in age, serum lipids platelet count or fibrinogen levels between the two groups. PDT was not significantly elevated in Group B vs Group A (103 ± 128 vs 84 ± 74 $\mu m^2/mm$, p = NS). PDT, however, was significantly augmented in patients with G > compared to <median (90 mg/dl) level (159 ± 141 vs 67 ± 69 $\mu m^2/mm$, $p < 0.01$).

Conclusion: Elevated G but not I is associated with augmented PDT in stable CAD patients with controlled lipid levels. This finding suggests that the mechanism contributing to the enhanced thrombogenic risk of CAD may be related to hyperglycemia rather than hyperinsulinemia.

1111-45 Thrombostatin, a PAR1 Inhibitor, Reduces Both Platelet Aggregation and Adhesion After Arterial Wall Injury With Balloon Angioplasty

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Background: Thrombostatin (TSTAT), the 1–5 (Arg-Pro-Pro-Gly-Phe) fragment of bradykinin, is a selective inhibitor of α-thrombin (IIa)-induced platelet (PLT) activation. This study examined the effects of TSTAT on PLT aggregation and adhesion following balloon angioplasty (BA).

Methods: Whole blood was collected from each of 16 Beagle dogs prior to sacrifice. PLT-rich plasma was labeled with ^{111}In. Carotid arteries (CAs) from each dog were isolated and mounted in a dual perfusion chamber. Both CAs were injured by a 3 mm balloon catheter and then perfused with ^{111}In-labeled PLTs with or without TSTAT for 60 min. Continuous measurement of particle size was made by a new method using the ratio of laser-light scattering at 1° to 5° spread on a diode array of a multichannel analyzer. This was confirmed by Coulter counter. Adhesion of ^{111}In-labled PLTs to the CAs was determined by radioactive counts measured in a γ-counter.

Results: The mean ratio of PLT aggregation in the perfusate (without and with TSTAT) by laser-light scattering was 1.4 (240.7 ± 80.3 vs. 177.8 ± 67.2; $p < 0.02$) and particle size by Coulter counter was 1.5 (39.9 ± 12.5 vs. 27.1 ± 11.5; $p < 0.01$), while the mean ratio of radioactive PLT adhesion was 2.3 (4,148.9 ± 947.9 vs. 1,779.8 ± 685.6; $p < 0.05$).

Conclusion: This study shows that TSTAT significantly decreased PLT aggregation and adhesion in dog CAs injured with BA.

1111-46 Is There a Difference in Thrombogenesis Between Patients With Paroxysmal, Persistent and Permanent Atrial Fibrillation?

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Background: Although chronic atrial fibrillation (AF) is known to be associated with a hypercoagulable state, it is uncertain whether the subgroups of chronic AF, namely paroxysmal, persistent or permanent AF differ in their thrombogenic potential.

Methods: We measured levels of von Willebrand factor (vWf IU/dL, a marker of endothelial dysfunction), soluble P-selectin (sP-sel ng/ml, an index of platelet activation) (both by ELISA) and fibrinogen (fib, g/L Clauss method) (all unaffected by warfarin) in 23 persistent AF patients taking warfarin (INR 2.0–3.0) (16 men; mean age 65 ± 13 years). Levels were compared to age- and sex-matched controls in sinus rhythm and with patients with paroxysmal and permanent AF (23 in each group and all fully anticoagulated).

Results:

	Controls	Paroxysmal AF	Persistent AF	Permanent AF	p+ values
sP-sel	34 (30–46)	36 (32–44)	51 (37–63)	210 (162–284)*	<0.001
vWf	101 ± 30	130 ± 34*	106 ± 26	143 ± 47*	0.018
Fib	2.5 ± 0.6	3.3 ± 0.7*	2.7 ± 0.8	3.1 ± 0.9*	0.077

*p < 0.005 paired t-test (controls *vs* AF); + oneway ANOVA (for paroxysmal, persistent and permanent AF) [Tukey's post hoc analysis: p = 0.013 for vWf and p < 0.001 for sP-sel between permanent and persistent AF; p < 0.001 for sP-sel between permanent and paroxysmal AF].

Conclusions: Permanent AF is associated with a hypercoagulable state (vWf, sP-sel and fibrinogen $p < 0.005$). Paroxysmal AF was found to have significantly raised levels of vWf and fibrinogen ($p < 0.005$) but not sP-sel. There were no significant differences in levels of fibrinogen, vWf and sP-sel between controls and patients with persistent AF (p = NS).

1111-47 Sustained Coronary Artery Recanalization With Adjunctive Infusion of a Novel P_{2T}-Receptor Antagonist AR-C69931 in a Canine Model

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Reperfusion therapy for acute MI remains limited by significant reocclusion rate due to excessive platelet accumulation and recruitment at the sites of vascular injury. We assessed the influence of a potent, specific, selective and novel P2T-receptor antagonist (AR-C69931), which inhibits ADP-induced platelet aggregation, in conjunction with thrombolytic therapy on the prevention of platelet aggregation and thrombosis formation in the canine model.

Methods: An electrolytic injury canine coronary thrombosis model was used in this study, including 20 hound dogs (20–22 kg) of either sex (AR-C69931 = 10, placebo = 10). A 2 cm segment of left circumflex coronary artery was isolated, and a doppler ultrasonic flow probe was placed around it for the measurement of coronary blood flow. Thrombosis was induced using the electrolytic injury technique. After thrombus formation, 30 min was allowed to elapse to confirm the stability of thrombosis. Ten minutes prior to administration of t-PA (1 mg/kg over 20 minutes), all animals received either saline or AR-C69931 (4 μg/kg/min) intravenously for total of 2 hours. All animals received heparin (80 U/kg) as bolus iv followed by a continuous infusion of 17 U/kg/hr.

Results: The incidences of reocclusion rate and cyclic flow variation were significantly decreased in the AR-C69931 group ($p < 0.05$) (Table). Platelet aggregation in response to ADP was decreased by half in the placebo group, but nearly 20-fold in the AR-C69931 group (1.11 ± 1.27 vs 10.25 ± 8.31 $p < 0.05$). At the end of adjunctive therapy, platelet aggregation in the AR-C69931 was decreased further (0.56 ± 1.33 vs 12.22 ± 11.48, $p < 0.05$). PT and aPTT were increased in all dogs as expected without a difference between two groups. BT was significantly extended by AR-C69931.

	RR	RT (min)	RD (min)	CFV	Reocclusion
Placebo	100%	21.5 ± 2.88	75 ± 39.86	50%	60%
AR-C69931	100%	20 ± 6.09	119.7 ± 0.67*	0%*	0%*

* P < 0.05 compared to placebo group. RR-Reperfusion rate; RT-Reflow time; RD-Reflow duration; CFV-Cyclic flow variation.

Conclusion: The administration of AR-C69931 in the canine coronary thrombosis model blocks ADP-mediated platelet activation, aggregation, and