(PTCA). Reducing platelet accumulation at PTCA sites may attenuate NP and restenosis. Single antiplatelet agents are not effective, due to multiple platelet activation pathways. Previous work suggested that combined antagonism of 2 mediators of platelet aggregation — thromboxane A_2 (by *ridogrel*) and serotonin (by *ketanserin*), could reduce platelet-thrombus formation and lessen NP. We therefore tested the hypothesis that combined treatment with 3 agents (*ridogrel, ketanserin,* and an ADP antagonist — *clopidogrel*) would be more effective in reducing NP after PTCA. We studied 18 dogs with coronary flow probes and plastic constrictors chronically implanted on LAD arteries. All dogs underwent LAD PTCA and were sacrificed after 8 weeks of monitoring. Eight dogs were controls, while 10 dogs were treated with combined antiplatelet therapy for 3 weeks before and 3 weeks after PTCA. Compared to controls, ex vivo platelet aggregation was virtually abolished in treated dogs, and bleeding times during treatment were greater (>720 vs 119 ± 4 sec, $p < 0.001$). Cyclic flow variations (CFVs) after PTCA, from repetitive accumulation and dislodgement of platelet aggregates at PTCA sites, occurred in 7/8 controls but in only 1/10 treated dogs ($p < 0.01$). Platelet counts and hematocrit values were not different between treated and control groups. Quantitative coronary artery histology revealed that neointimal area was threefold less in the treated group (0.18 ± 0.07 cm^2 vs 0.52 ± 0.12, $p = 0.032$), as was the percent lumen stenosis (13 ± 4% vs 40 ± 13%, $p = 0.06$).

Conclusion: Combination antiplatelet therapy with these 3 antagonists inhibited several relevant measures of platelet function and reduced neointimal proliferation in a canine coronary artery angioplasty model.

2:30

751-3 Lovastatin and Probucol for the Prevention of Restenosis After Coronary Angioplasty

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We hypothesized that combination lipid lowering therapy (Lovastatin) and anti-oxidant (Probucol) therapy might reduce restenosis following coronary angioplasty (PTCA). To address this question, 239 patients (pts) were enrolled in a multi-center, randomized trial whereby 2 out of 3 pts received Lovastatin 20 mg bid and Probucol 500 mg bid in combination; 1 out of 3 pts was randomized to double placebo. Pts were treated in a blinded fashion for 6 months. Total cholesterol (154 vs 211), LDL (98 vs 141) and HDL (31 vs 42) were lower in treated compared with placebo patients. Serious adverse effects from the medications were not observed.

EVENTS WITHIN 6 MONTHS

	Active (n = 163)	Placebo (n = 76)
Death	1 (1%)	1 (1%)
Myocardial Infarction	3 (2%)	1 (1%)
Repeat PTCA	51 (31%)	22 (29%)
Bypass Surgery	7 (4%)	3 (4%)

Quantitative coronary angiography was available in 147 lesions, the mean loss in luminal diameter was 27% ± 31% and 28% ± 34% in treated and placebo groups.

Conclusion: Combination Lovastatin and Probucol: 1) reduced total cholesterol (27%), LDL (29%) and HDL (27%) levels, but 2) did not prevent restenosis or clinical events during the first six months post-angioplasty.

2:45

751-4 Low Molecular Weight Heparin in the Prevention of Restenosis After Coronary Angioplasty. Results of the FACT Study

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Restenosis after coronary angioplasty is a multifactorial process that may involve elastic recoil, thrombus incorporation, smooth muscle cell proliferation, and late vascular remodeling. Fraxiparine (nadroparin) is a low molecular weight heparin derivative that has potent antithrombotic and antiproliferative properties in animal models.

The FACT (Fraxiparine Angioplastie Coronaire Transluminale) study is a multicentre double-blind randomised trial designed to compare the effects of treatment with Fraxiparine or aspirin on the occurrence of restenosis after coronary balloon angioplasty. All patients received aspirin (250 mg, daily) before coronary angioplasty. Therapeutic doses of unfractionated heparin were used during coronary angioplasty in both groups. The active treatment group received subcutaneous injections of Fraxiparine (0.6 ml) daily for 3 days before coronary angioplasty that was continued for 3 months. The control group was treated with aspirin (250 mg) daily for 3 months.

In total, 354 patients were randomized and constitute the intention-to-treat population. Angiographic follow-up was performed in 91% of patients with successful procedures at 3 months. There were no differences between groups in baseline clinical characteristics. The acute gain (0.96 ± 0.42 mm, 1.03 ± 0.40 mm) and late loss (0.36 ± 0.51 mm, 0.36 ± 0.57 mm) were similar in the Fraxiparine and aspirin groups. Restenosis, defined as a binary variable (stenosis >50% at angiographic follow-up) occurred in 41% of the Fraxiparine treated and 38% of the aspirin treated group ($p = 0.69$). At six months major clinical event rates, death (1% vs 2%), acute myocardial infarction (4% vs 2%) and repeat revascularization (26% vs 26%) were similar in both groups.

Despite, 3 days of pretreatment and 3 months of treatment with low molecular weight heparin (Fraxiparine), no statistical differences were observed in angiographic or clinical end points.

3:00

751-5 Rapid Angiographic Progression of "Target" and "Non-target" Stenoses in Patients Awaiting Coronary Angioplasty

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Coronary angioplasty (PTCA) is effective therapy for angina pectoris but coronary events occur after successful PTCA which may be caused by both restenosis and progression of mild pre-existing, *"non-target"*, stenoses. To compare the short-term evolution of *"target"* versus *"non-target"* stenoses in patients awaiting PTCA, we prospectively studied 161 consecutive stable angina patients (124 men and 37 women). After diagnostic angiography, *"target"* stenoses for PTCA and *"non-target"* lesions were identified. Patients were put on a routine waiting list and followed up regularly until repeat coronary arteriography (mean ± SD: 7 ± 3 months), which was performed immediately preceding angioplasty (138 patients) or soon after acute coronary events (23 patients) when these occurred. Stenosis diameters were measured using computerized arteriography. Progression was defined as ≥20% diameter reduction, new total occlusion, or development of "new" stenoses ≥30%. At study entry, diameters of *target* (n = 207) and *non-target* (n = 184) lesions were 68 ± 9% and 38 ± 9%, respectively ($p < 0.001$). Disease progression occurred in 33 patients (20%), in whom 18 *target* (9%) and 15 *non-target* stenoses (8%) progressed and 7 new lesions (1 total occlusion) developed. Total occlusion developed in 15 of the 18 (83%) *target* and in 6 of the 15 (40%) *non-target* stenoses; ($p = 0.03$). During follow up, 3 patients (2%) had a myocardial infarction and 20 (12%) developed unstable angina. These events were associated with progression of *target* stenoses in 10 patients, of *non-target* stenoses in 7 patients, and with new lesions in one patient. In 5 patients events were not associated with stenosis progression.

Thus a similar proportion of *target* and *non-target* lesions progressed rapidly. *Target* stenoses, however, were more likely to progress to total occlusion than *non-target* lesions. Progression of *non-target* stenoses may contribute to recurrence of angina and new coronary events after successful angioplasty and their role should be considered when developing strategies aimed at improving survival after angioplasty.

3:15

751-6 Multiple Repeat Coronary Angioplasty for Final Lesion Patency

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To demonstrate that multiple repeat coronary angioplasty can be solely utilized to achieve final lesion patency after restenosis, such a protocol was prospectively applied for restenosis since 1983. Bypass surgery was only considered for 1) new left main trunk lesions, 2) symptomatic restenosis where angioplasty was either unsuccessful or unsuitable, and 3) patient preference. Between 1983 and 1992, 1455 lesions (acute myocardial infarction or total occlusion excluded) were successfully dilated for the first time. Although only 941 (68%) of the 1385 lesions studied showed satisfactory patency (≤70% stenosis) after the first procedure, 93% (1248/1345 studied) showed satisfactory patency after repeating angioplasty up to 3 times and 94% (1268/1354 studied) after repetition up to 6 times. Only 23 lesions (1.6%) required 4 or more procedures and 20 of them showed final patency. Disease aggravation (either impossible or failed repeat angioplasty, acute infarction, or sudden death) occurred in 43 lesions (3.2%). Bypass grafts were done for 11 lesions of 7 patients, mostly due to disease progression at the left main trunk.