moting local thrombogenesis (mortality at 14 days 22% versus 10%, p = 0.026). Interestingly, this difference in mortality was almost entirely observed within the subgroup of patients treated with heparin alone instead of thrombolysis or embolectomy as adjuncts to heparin (25% versus 7.2%, p=0.007), despite similar clinical severity at presentation (systolic blood pressure 122.2±24.2 versus 127.8±24.1 mmHg, hypotension in 5.9% versus 3.4%, and right ventricular hypokinesis in 52.5% versus 30.8% patients, respectively, all differences non-significant).

Conclusions: RHTh confer an ominous prognosis with increased early mortality, especially evident in patients treated with heparin alone. These findings suggest that patients with acute PE who have RHTh should be managed with more aggressive therapy than heparin anticoagulation alone, even when hemodynamically stable at the time of presentation.

4:30 p.m.

873-3 Comparison of Narrow Versus Standard Target INR Ranges

David J. Meier, Seema S. Sonnad, Julie C. Merz, William P. Fay, *University of Michigan, Ann Arbor, Michigan.*

Background: Although current guidelines suggest a target INR range of 2.0-3.0 or 2.5-3.5 for most patients, physicians frequently select narrow target INR ranges (e.g. 2.0-2.5) in an attempt to minimize complications. However, the efficacies of narrow versus standard target INR ranges are unknown. We hypothesized that narrow range management results in a greater frequency of INRs <2.0 or >4.0, which are associated with an increased risk of thrombotic and bleeding complications, respectively.

Methods: We identified 32 patients managed with both a narrow and a standard range strategy during their course of anticoagulation. Over 3000 INRs during 133 patient-years of follow-up were obtained. Sixteen patients were managed with both a 2.0-3.0 and a 2.0-2.5 range (Group A) and 16 patients were managed with both a 2.5-3.5 and a 3.0-3.5 range (Group B).

Results: Blood draws per month were more frequent (2.0±0.2 vs. 1.7±0.1; p=0.035) during narrow range management for both groups combined. For Group A, mean INR was lower (2.4±0.03 vs. 2.6±0.06; p<0.02) and frequency of INRs <2.0 was higher (23.6±2.4 vs. 17.2±2.7; p<0.04) during narrow range management. For Group B, mean INR was higher (3.4±0.03 vs. 3.1±0.06; p<0.001) and frequency of INRs >4.0 was higher (21.2±1.4 vs. 13.0±2.3; p<0.007) during narrow range management.

Conclusions: Compared to a target INR range of 2.0-3.0, management with a target range of 2.0-2.5 increases the frequency of INRs <2.0, which are associated with an increased risk of thrombotic complications. Conversely, compared to a target range of 2.5-3.5, management with a target range of 3.0-3.5 increases the frequency of INRs >4.0, which are associated with a significantly increased risk of hemorrhagic complications. Narrow target INR ranges also increase the cost and patient inconvenience associated with anticoagulant therapy. Physicians should take these issues into account before selecting narrow target INR ranges for their patients.

4:45 p.m.

873-4 Alteplase Improves the Clinical Course of Patients With Major Pulmonary Embolism: A Multicenter, Randomized, Placebo-Controlled Trial (Management Strategies and Prognosis in Pulmonary Embolism Study 3)

Stavros Konstantinides, Annette Geibel, Wolfgang Kasper, *University of Goettingen, Department of Cardiology and Pulmonary Medicine, Goettingen, Germany, St. Josefs Hospital, Wiesbaden, Germany.*

Background: The clinical benefit of thrombolytic treatment in patients with major pulmonary embolism (PE) who appear stable at presentation remains highly controversial.

Methods: In a prospective, multicenter, placebo-controlled trial, 250 consecutive patients with PE confirmed by lung scan, spiral CT, or pulmonary angiography were enrolled and 247 of them randomly assigned to treatment with alteplase (100 mg infusion over 2 h) plus heparin or heparin alone. Patients had major PE defined as 1) echocardiographic findings of right ventricular enlargement and/or pulmonary hypertension; 2) new-onset right heart strain on the ECG; or, 3) precapillary pulmonary hypertension on Swanz-Ganz catheterization. Patients with peristent arterial hypotension, cardiogenic shock, or need for cardiopulmonary resuscitation (CPR) at presentation were excluded. The primary end point was 30-day mortality or escalation/change of therapy (defined as need for breaking the code and/or one of the following: catecholamine infusion, endotracheal intubation, CPR, or emergency thrombolysis, catheter fragmentation, or surgical embolectomy) at least 2 h after randomization.

Results: Alteplase was given to 115 (47%) and heparin alone to 132 (53%) pts. No differences existed between the 2 groups with regard to the clinical symptoms, physical examination, radiologic, ECG, echocardiographic, or laboratory findings at randomization. The primary end point was reached in 31 pts (24%) of the heparin group compared with only 14 (12%) of those in the thrombolysis group (p=0.021). This difference was largely due to the more frequent need for escalation of therapy in the heparin vs. thrombolysis group (24 vs. 11%; p=0.01), since mortality was low in both groups (2 and 4 pts respectively; p=0.42). Major bleeding was 3% in the heparin and 0.9% in the alteplase group (p=0.38), whereas hemorrhagic stroke occurred in only 1 patient (0.8%) in each group.

Conclusion: In this largest to-date randomized trial of thrombolysis vs. heparin for PE, alteplase was found to favorably affect the clinical course of pts with major PE appearing hemodynamically stable at presentation, although it did not reduce in-hospital mortality.

ORAL CONTRIBUTIONS

881 Inflammation and Inflammatory Markers

Wednesday, March 20, 2002, 8:30 a.m.-10:00 a.m.
Georgia World Congress Center, Room 254W

8:30 a.m.

881-1 The Association Between Inflammatory Markers and Thrombogenic Factors in Postinfarction Patients

Tareq S. Harb, Wojciech Zareba, Arthur J. Moss, Paul M. Ridker, Nader Rifai, Victor J. Marder, Luc Miller-Watelet, *University of Rochester Medical Center, Rochester, New York.*

Background: Dyslipidemia, inflammation and thrombosis are all implicated in the pathophysiology of plaque instability and rupture. To better understand the association among these mechanisms, we investigated the relationship between levels of inflammatory markers C-reactive protein (CRP) and serum amyloid A (SAA) and thrombogenic and lipid factors in patients with established coronary artery disease.

Methods: Blood levels of CRP, SAA and various thrombogenic and lipid factors were measured 2 months after an index myocardial infarction in 957 patients. Multivariate analyses were used to determine the relationship between levels of inflammatory markers and levels of lipid and thrombogenic factors.

Results: In multivariate analysis, elevated CRP and SAA (≥75th percentile) were associated with increased levels (p<0.001) of several thrombogenic factors as summarized in the table below. Conversely, neither inflammatory marker was significantly associated with levels of lipid factors.

Conclusion: In stable post-infarction patients, there is a significant association between levels of inflammatory markers and thrombogenic factors. Conversely, levels of inflammatory markers are not significantly associated with the degree of dyslipidemia. This data suggests a possible mechanistic relationship between inflammation and thrombosis in patients with established coronary artery disease.

	Elevated CRP		*Elevated SAA*	
	OR	**CI***	**OR**	**CI***
vWF	2.21	1.50-3.25	2.79	1.88-4.14
Fibrinogen	1.013	1.011-1.016	1.010	1.008-1.012
D-Dimer	1.85	1.46-2.35	2.10	1.65-2.68

* - p<0.001
vWF - von Willebrand Factor
CI - 95% Confidence Interval
OR - Odds Ratio (expressed per 1 log unit increase in vWF and D-Dimer and per 1 mg/dl % increase in fibrinogen)

8:45 a.m.

881-2 C-Reactive Protein Predicts Microalbuminuria

Adrian W. Messerli, Ravish Sachar, Gregory L. Pearce, Byron J. Hoogwerf, Dennis L. Sprecher, *The Cleveland Clinic Foundation, Cleveland, Ohio.*

Background: Inflammation leads to endothelial dysfunction. It has been proposed that endothelial changes can lead to small losses of protein from the renal glomeruli. If C-reactive protein (CRP) is a marker for inflammation, then it may predict microalbuminuria.

Methods: We analysed serum CRP and urine albumin/ creatinine ratios (ACR) from 343 patients (n=52, diabetics) drawn from our preventive cardiology clinic. ACR values >20 mg/g were used as the cutpoint, approximating the upper quartile presented in the HOPE trial. Quintiles of CRP from our population were utilized. **Results**: Logistic regression models were constructed to determine the relative risk of microalbuminuria associated with each quintile increase in CRP. Three models were run: (1) unadjusted, (2) Framingham adjusted, and (3) Framingham + CAD status adjusted. All three models show that CRP partially explains the level of microalbuminuria for each successive CRP quintile (see table). In contrast to a previous cohort analysis, further adjustment for fibrinogen, waist, and glucose level did not change the outcome. **Conclusions**: Each progressively higher CRP quartile predicts an additional 30% risk for the presence of microalbuminuria. These data are consistent with and further substantiate the relationship between inflammation and renovascular endothelial dysfunction.

Logistic regression of RR for ACR >20 mg/g

	DM		ALL	
	OR (95% C.I)	p-value	OR (95% C.I.)	p-value
Unadjusted	2.08 (1.18-3.68)	0.01	1.38 (1.12-1.72)	0.003
Framingham Adjustment	2.06 (1.16-3.66)	0.01	1.31 (1.05 - 1.63)	0.02
Framingham + CAD	2.05 (1.15-3.67)	0.02	1.32 (1.05-1.66)	0.02