(21%) patients. Peri-procedural bradycardia occurred in 99 (24.5%) patients but only 61 (15%) required atropine. Patients with HI had a significantly increased risk of stroke (OR=2.6, 95% CI 1.2-5.9), myocardial infarction (MI) (OR=4.5, 95% CI 1.2-16.9) or death (OR=2.7, 95% CI 1.0-7.6) in the peri-operative period. The odds ratio for the combined endpoint of stroke, MI or death was 3.6 (95% CI 1.8-6.9) in patients with HI.
Conclusions: HI is common after CAS and often requires pharmacological intervention. Patients with HI are at an increased risk for stroke, MI or death and require close monitoring.

Noon

1116-5 **Elevated Preprocedural C-Reactive Protein Levels Predict Death and Stroke in Patients After Carotid Artery Stenting**

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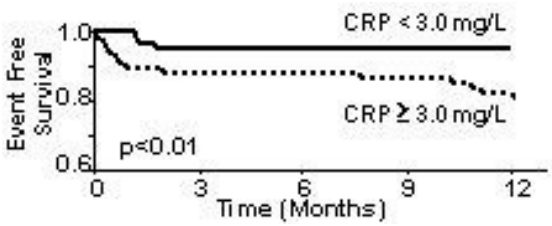
Background: Elevated pre-procedural C-reactive protein (CRP) levels are associated with the composite endpoint of death or myocardial infarction in patients undergoing percutaneous coronary intervention.We sought to determine whether elevated pre-procedural CRP levels predict the composite endpoint of death or stroke in patients who undergo carotid artery stenting.
Methods: Between December 1999 and August 2002, we examined 133 patients with pre-procedural CRP levels who underwent carotid artery intervention from a carotid interventional registry. Using a CRP level of 3.0 mg/L as the cutoff, patients were sub-divided into high CRP (n=67) and low CRP (n=66) groups. The 30 day and 12 month composite endpoint of death or stroke were compared between the groups.
Results: No significant differences in baseline demographics were found between the two groups (including age, gender, coronary artery disease, or prior stroke or transient ischemic attack), except for hyperlipidemia which was significantly higher in the low CRP group. For the entire cohort, the death/stroke rates at 30 days and 12 months were 5% (7 events) and 12% (16 events) respectively. The 30 day death/stroke rate was significantly higher in the high CRP group vs. the low CRP group (10% vs. 0%, p<0.01). This increased event rate was sustained at one year (19% vs. 5%, p<0.01).
Conclusion: In patients who undergo carotid artery stenting, pre-procedural CRP levels predict the composite endpoint of death or stroke at 30 days and 12 months.



Noon

1116-6 **Long-Term Clopidogrel Therapy Following Percutaneous Coronary Intervention Improves Clinical Outcome but Is Not Associated With Increased Bleeding: New Insights From the CREDO Trial**

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Background: In the CREDO trial, the 1-year incidence of major adverse clinical events (MACE) among patients undergoing or likely to undergo coronary stenting was significantly reduced by a pre-procedure clopidogrel loading dose plus 1 year of clopidogrel compared with no loading dose and 28 days of clopidogrel. Because most patients undergoing coronary stenting receive 4 weeks of dual antiplatelet therapy with aspirin and clopidogrel, we sought to determine predictors of bleeding and occurrence of major events between day 29 and 1 year among patients enrolled in the CREDO trial.
Methods: Patients who survived to day 29 were included (n=2068) in this intent-to-treat analysis. Minor and major bleeding events (TIMI criteria) were pooled into a composite of any bleeding. MACE was a composite of death, non-fatal myocardial infarction (MI) and stroke.
Results: From day 29 through 1 year there were 138 bleeding events, 68 in the clopidogrel and 70 in the placebo arm (p=0.84). Of these, 112 (81%) were procedure-related, and most (82, 59%) occurred in the setting of coronary artery bypass graft surgery (CABG). In a multivariable model including demographics, comorbidities and concomitant medical therapies, the only significant independent predictors of bleeding were increasing age, diabetes (DM), and CABG (model chi square 398, p < 0.001, c statistic 0.85); clopidogrel therapy beyond 28 days was not a significant predictor of major or minor bleeding. During that same interval, 80 MACE occurred. First MACE was significantly less frequent among those randomized to clopidogrel than placebo (3.0 vs. 4.7%, p=0.043).
Conclusions: With the sustained use of dual antiplatelet therapy from 1 month to one year after percutaneous coronary intervention, there is a significant 36% reduction of death, MI, and stroke without any increase in bleeding events.

Noon

1116-7 **Similar Outcomes Between Patients With Native Coronary and Bypass Graft Disease Treated With Sirolimus-Eluting Stents in the SECURE Trial**

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Background: Bare metal stenting or CABG has provided limited success for the treatment of bypass graft disease. The efficacy of Sirolimus-eluting Bx Velocity stents (SES) in native coronary arteries is proven, however its application in bypass grafts remains unknown. We compared the long-term results between patients with native coronary disease versus those with graft disease treated with sirolimus-eluting stents as part of SECURE trial.
Methods and Results: Patients (n=252) with a serious disease or condition for which there was no acceptable alternative treatment available were enrolled. Out of 202 patients with complete 6-month follow-up, 58 patients had 75 graft lesions (GI) and 144 patients had 286 lesions in native vessels (GII). There were more males in GI(83%) versus GII (67%). Other baseline characteristics were similar, with 39% diabetics in each group. 71% of lesions in GI and 58% of lesion in GII were treated with previous brachytherapy. All patients received aspirin and clopidogrel for at least 6 months. Angiographic vessel diameter, determined by the core lab, was larger in GI (2.26mm) versus GII (1.92mm). Likewise, in-stent MLD post procedure was 2.52mm (GI) and 2.18mm (GII). Mean total stent length was 23.3mm in both groups. There was no in-hospital adverse event in GI and 1 death (0.7%) in GII. After 6 months, 13.8% of patients in GI versus 10.4% of patients in GII had at least one major adverse event (death, myocardial infarction, target lesion revascularization or emergent CABG). TVR rate was 12.1% in GI and 9% in GII. Updated data with angiographic follow-up will be available for presentation.
Conclusion: In the SECURE trial, which enrolled a very high risk group of patients, the use of sirolimus-eluting stent to treat bypass graft disease was feasible, safe and provided acceptable long-term results compared to the outcomes of patients with native coronary disease.

Noon

1116-8 **Early and Mid-Term Results of Cypher Stents in Unprotected Left Main**

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The safety and efficacy of percutaneous coronary intervention in unprotected left main (ULM) coronary arteries confronts with the problems associated with restenosis.
Methods From April 2002 32 consecutive patients were electively treated in our instution with the implantation of Cypher (Cordis, Johnson and Johnson Company, Warren, NJ)Sirolimus-eluting stent (SES) in unprotected left main.
Results 4 patients (12.5%) were diabetics, 7 (22%) had unstable angina, mean age was 58±13 **y**ears, and EF was 51± 6.6 %. The site of the lesion in LM was ostial in 3 (9.3%) patient, mid-portion of the artery in 3 patients (9.3%) and distal in 27 (84.3%) patients (bifurcation in 21pts and trifurcation in 6). In 19 (70%) patients with distal LM disease both branches were stented with SES, kissing balloon inflation was performed in 15 (55.5%). Only POBA in side branch was performed in 3 patients (11%), 5 pts had no treatment in the side branch. The largest nominal diameter of SES available was 3.0 mm (6 cells). Angiographic as well as procedural success was achieved in all patients. Elective intra-aortic balloon pump was used in 4 patients and GP IIb/IIIa antagonists were used in 16 (50 %) patients. During hospitalization, no patient died, nor had myocardial infarction (MI) or CABG , one patient had repeated PTCA due to residual dissection distal to the Cypher stent. At 6 month clinical follow-up 1 patient died after discontinuing antiaggregant theraphy because of acute pancreatisis, 6 (18.7%) patients had TLR (4 re-PCI and 2 CABG) and 1 had MI. Angiographic follow-up was achieved in 23 pts (74%). Restenosis occurred in 6 patients; all restenostic lesions were located in the distal LM.
Conclusions In this early experience with Cypher stents in ULM we can state that the problem of in-stent restenosis is still present mainly at the level of the bifurcation. We can speculate that the usage of 3 mm stents (6 cells) in vessels usually larger than 3.5mm could have contributed to inhomogeneous drug delivery to the vessel wall.

Noon

1116-9 **Trends in Fibrinolytic Therapy and Intra-Aortic Balloon Pump Counterpulsation Utilization in Patients With Cardiogenic Shock Complicating Acute Myocardial Infarction in Hospitals Without Percutaneous Transluminal Coronary Angioplasty/Coronary Artery Bypass Graft Capability: Observations From the National Registry of Myocardial Infarction**

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Background: Treatment of patients (pts) in cardiogenic shock (CS) complicating acute myocardial infarction (AMI) with fibrinolytic therapy (FT) and intra-aortic balloon pump counterpulsation (IABP) in hospitals without PTCA/CABG capability is associated with mortality reduction.
Objectives: We determined trends in utilization of FT, IABP, and mortality rates for patients in CS complicating AMI in the National Registry of Myocardial Infarction (NRMI) population for hospitals without PTCA/CABG capability.

Methods: From 07/94 to 10/01 the NRMI accrued 3,768 pts with AMI complicated by CS from 980 hospitals without PTCA/CABG capability. Trends in baseline characteristics, in-hospital mortality, transfer rates to hospitals with PTCA/CABG capability, and management patterns were evaluated.
Results: The mean age of the group was 71.3 ± 12.5 years. There were no differences over time in age, % women, stroke, and prior CABG. There were fewer pts in recent years with history of MI (p<0.001), but more pts with prior PTCA, CHF, HTN and dyslipidemia (p<0.05). There was a trend of reduction in use of FT from 39.5% to 31.4% (p=0.05), and very low rates of IABP use that did not change over time (5.7% to 5.3%, p= N.S.). Mortality was very high and unchanged over time (84.5% to 85.2%, p=N.S.). Overall transfer-out rates increased (p<0.0001) from 27.7% to 33.9%. However, transfer-out rates remained relatively flat over last 4 years (32.7%, 33.3%, 34.8%, 33.9%, respectively), with mortality rates increasing over that time period (81.2%, 83.9%, 85.3%, 85.9%, respectively), but FT rates continued to decrease (36.2%, 38.2%, 36%, 31.4%, respectively).
Conclusion: FT and IABP were underutilized in hospitals without PTCA/CABG capability. Mortality was very high and unchanged over time. Furthermore, FT utilization was decreasing despite the fact that transfer out rates remained unchanged over the last several years. Overall, most registered pts did not receive FT or IABP, and were not transferred out to hospitals with PTCA/CABG capability. For hospitals without PTCA/CABG capability we recommend an early FT and IABP, followed by immediate transfer to regional centers for revascularization for patients < 75 years of age.

Noon

1116-10 Shock in Patients With Acute Aortic Dissection: Clinical Characteristics, Risk Factors, and Outcomes

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Background: Shock often complicates acute aortic dissection (AAD). However, the clinical characteristics, risk factors and outcomes of shock in patients with AAD are not known. ***Methods*****:** Accordingly, we studied 1073 AAD patients enrolled in the International Registry of Acute Aortic Dissection (IRAD) between 1996 and 2001. ***Results:*** Shock occurred in 313 (29.2%) AAD patients (46.0% on admission and in the remaining after admission) and was more common in patients with acute type A than type B dissection (37.9% vs. 14.6%, p<0.0001). The proportion of patients with shock increased with advancing age (p for trend =0.043). Multivariate logistic regression identified age ≥70 years (OR, 2.0; 95% CI, 1.4-2.9; P<0.0001), type A dissection (referent type B AAD, OR 2.1, 95% CI, 1.4-3.2, p=0.0002), neurologic deficit (OR 3.8; 95% CI, 2.2-6.6; P<0.0001), syncope (OR 2.9; 95% CI, 1.8-4.7; P<0.0001), aortic regurgitation requiring valve surgery (OR 1.9, 95% CI 1.1-3.3, P=0.024), cardiac tamponade (OR 5.1, 95% CI 3.0-8.8, P<0.001) and new Q wave or ST segment deviation on ECG (OR 1.6; 95% CI, 1.1-2.4; P=0.014) as independent associations of shock (c-statistic 0.78, Hosmer Lemeshow χ^2 5.78, degrees of freedom 8, p=0.67). To validate our model and examine its ability to discriminate, we used the bootstrap resampling technique, and calculated the ROC curves of 1000, 100% samples of data with replacement. The area under the average curve was 0.79 (95% CI 0.75 to 0.82), indicating a good ability of the model to discriminate between patients with AAD who had shock and those who did not. Hospital complications (neurological deficits [22.7% versus 12.0%], altered mental status [26.1% versus 4.4%], myocardial [14.6% versus 6.9%], mesenteric [6.9% versus 2.6%] or limb ischemia [14.6% versus 6.9%]); and death [55.0% versus 10.3%] occurred more frequently in patients with shock than in those without it (P<0.001 for all comparisons). ***Conclusions:*** Shock occurred in more than a quarter of AAD patients and was associated with a much higher in-hospital adverse event rate. Our study identified factors associated with shock in AAD patients. Knowledge of these associations may be useful to clinicians as they triage and treat patients with AAD.

Noon

1116-11 The Mineralocorticoid Paradox: Profibrotic In Vivo in Experimental Asymptomatic Left Ventricular Dysfunction but Antifibrotic In Vitro

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Background: Asymptomatic left ventricular dysfunction (ALVD) has maintenance of sodium (Na) excretion and activation of natriuretic peptides (NP), but not aldosterone (ALDO). Normal subjects escape the Na and water retaining effects of exogenous deoxycorticosterone acetate (DOCA), an ALDO precursor. Overt congestive heart failure (CHF) cannot escape ALDO or DOCA's actions, resulting in worse edema. ALDO may cause cardiac hypertrophy and fibrosis. In clinical trials ALDO antagonism benefited CHF patients perhaps due to antifibrotic effects. ALVD's response to DOCA excess is unknown. We hypothesized that: (1) in ALVD exogenous DOCA would result in Na and fluid retention, (2) DOCA excess in ALVD would give cardiac fibrosis, and (3) collagen synthesis would increase in cardiac fibroblasts (CF) incubated with ALDO.
Methods: Cardiorenal function was assessed in two groups of ALVD dogs induced by 180 bpm tachypacing. One group was a control (A); the other (A+D) received DOCA (1 mg/kg/d i.m.) starting pacing day 2. Collagen area fraction was measured in picrosirius red stained left ventricle. The effect of ALDO (10-9 M, 10-6 M) on DNA and collagen syntheses in canine CF from normal left ventricle was determined by [3H]-thymidine and [3H]-proline incorporation.
Results: Urinary flow (UVolR) and Na excretion (UNaV) were unchanged in A, with no ALDO activation. In contrast, in A+D UNaV decreased the first two days DOCA was given, but normalized on day 4 despite continuing DOCA. Increased UVolR and urinary cGMP excretion occurred with DOCA escape. No differences in cardiorenal parameters existed on day 11. Collagen area fraction in A+D was significantly higher than in A, 3.6±0.4% vs 2.0±0.2% (p=0.02). Conversely, ALDO (10-6M) added to CF decreased [3H]-proline and [3H]-thymidine incorporation (both p<0.01).
Conclusion: ALVD escapes DOCA's Na retaining effects. Despite A+D's renal escape, this group had more cardiac fibrosis than A. Hence, the heart did not escape DOCA's tissue effects. However, ALDO failed as a direct stimulator of collagen synthesis in CF. This paradox of mineralocorticoid induced fibrosis *in vivo* but not *in vitro* suggests that ALDO's profibrotic effects require another factor's presence.

Noon

1116-12 PG-530742, a Novel Matrix Metalloproteinase Inhibitor, Improves Left Ventricular Function and Attenuates Remodeling in Dogs With Chronic Heart Failure

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Background: PG-530742 (PG) is a hydroxamic-based matrix metalloproteinase (MMP) inhibitor that is 2 to 3 orders of magnitude more potent as an inhibitor of MMP-2, -3, -8, -9, -13 and -14 than MMP-1 and -7. This study examined the effects of chronic monotherapy with PG on LV function and remodeling in dogs with coronary microembolization-induced heart failure (HF). **Methods:** A blinded, randomized, placebo-controlled design was used. Dogs were randomized to 3 months therapy with low dose (LD) PG (0.2 mg/kg, tid, n=8), high dose (HD) PG (3.5 mg/kg, tid, n=8) or placebo (PL) (vehicle, tid, n=8). LV ejection fraction (EF), end-diastolic (EDV) and end-systolic volumes were measured from ventriculograms at time of randomization (PRE) and after 3 months of therapy (POST). At POST, hearts were removed and LV tissue used to measure cardiomyocyte cross-sectional area (MCSA), a measure of myocyte hypertrophy and volume fraction of interstitial fibrosis (VFIF). **Results:** In PL-treated dogs, EDV and ESV increased and EF decreased (Table). LD-PG elicited changes similar to PL. In contrast, HD-PG decreased EDV and ESV and increased EF. MCSA was not different with LD-PG compared to PL (737 ± 28 vs 688 ± 26 um^2) but decreased with HD-PG (498 ± 22 um^2, P<0.05). VFIF was not different with LD-PG compared to PL (15 ± 1 vs 14 ± 1 %) but decreased with HD-PG (10 ± 1 %, P<0.05). **Conclusions:** In dogs with HF, chronic therapy with HD-PG improves LV function and attenuates LV remodeling. PG may be useful as adjunct therapy for treatment of chronic HF.

	Placebo		LD-PG-530742		HD-PG-530742	
	PRE	POST	PRE	POST	PRE	POST
EDV (ml)	57 ± 2	63 ± 2*	58 ± 2	63 ± 2*	59 ± 4	57 ± 4*
ESV (ml)	36 ± 1	42 ± 2*	38 ± 2	43 ± 2*	38 ± 2	34 ± 2*
EF (%)	36 ± 1	33 ± 1*	35 ± 1	31 ± 1*	36 ± 1	40 ± 1*

*=p<0.02 PRE vs. POST

Noon

1116-13 Chronic Therapy With Eplerenone Reduces Tubulin-Alpha and -Beta mRNA Expression and Increases Titin mRNA Expression in Dogs With Heart Failure

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Background: Titin, a cytoskeletal protein that ensures elasticity and extensibility of the sarcomere is decreased in heart failure (HF) leading to increased LV stiffness. Tubulin (TU), a cytoskeletal protein consisting of an alpha and a beta isoforms increases in HF and can lead to contractile dysfunction and loss of compliance. We previously showed that eplerenone (EPL), a new aldosterone receptor blocker, reduces LV end-diastolic wall stress, stiffness and improves relaxation in dogs with HF. This study examined the effects of EPL on titin and TU-alpha and -beta mRNA expression in LV tissue of dogs with coronary microembolization-induced HF. **Methods:** Dogs were randomized to 3 months therapy with EPL (10 mg/kg Bid, n=7) or to no therapy (control, n=7). Tissue from 6 normal (NL) dogs was used for comparison. LV tissue from all dogs was used to extract RNA. mRNA expression for titin and TU was measured using reverse transcriptase polymerase chain reaction and bands quantified in densitometeric units. **Results:** Data shown in table. Compared to NL, titin mRNA expression decreased in controls and returned to near NL with EPL. mRNA expression for TU-alpha and -beta increased in controls compared to NL and returned to near NL with EPL. **Conclusions:** In dogs with HF, mRNA expression for titin is decreased and mRNA expression for TU-alpha and -beta is increased. EPL therapy normalized expression of both genes. This restoration of key cytoskeletal proteins partly explains the improvement in LV diastolic function seen with EPL.