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

Thomas T. Tsai, Eric M. Isselbacher, Christoph A. Nienaber, Arturo Evangelista, Jianming Fang, Dean E. Smith, Jeanna V. Cooper, Stuart Hutchison, Eduardo Bossone, Patrick O'Gara, Kim A. Eagle, Rajendra H. Mehta, On behalf of the International Registry of Acute Aortic dissection, University of Michigan, Ann Arbor, MI

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

Lisa C. Costello-Boerrigter, Guido Boerrigter, Gail J. Harty, Alessandro Cataliotti, Denise M. Heublein, Sharon M. Sandberg, John A. Schirger, Fernando L. Martin, Margaret M. Redfield, John C. Burnett, Jr., Mayo Clinic and Foundation, Rochester, MN

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

Hani N. Sabbah, Hideaki Morita, George Suzuki, Victor G. Sharov, Anastassia Todor, Timothy P. O'Neill, Henry Ford Health System, Detroit, MI, Procter and Gamble Pharmaceuticals, Mason, OH

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

Sharad Rastogi, Sudhish Mishra, Ramesh Gupta, George Suzuki, Hideaki Morita, Sidney Goldstein, Hani N. Sabbah, Henry Ford Health System, Detroit, MI

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.