852 The Hemodynamics of Mitral Valvular Heart Disease: Influence of Pharmacology and Physiology

Tuesday, March 31, 1998, 2:00 p.m.–3:30 p.m.
Georgia World Congress Center, Room 364W

2:00

852-1 A Prospective Trial on the Effects of Losartan on the Degree of Mitral Regurgitation

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Vasodilators have been used clinically in pts with mitral regurgitation (MR), but their efficacy in reducing volume overload caused by MR is not quantitatively documented. In a prospective pilot trial, 29 pts (23 men, age 68 ± 14) underwent a quantitative echocardiogram at baseline and four hours after 50 mg losartan orally. The regurgitant volume (RVol) and effective regurgitant orifice (ERO) were quantified using two methods (flow convergence and quantitative Doppler). Measurements included indexed left ventricular end-diastolic (EDVI) and end-systolic volumes (ESVI), ejection fraction (EF) and mean blood pressure (MBP). In 24 pts, the echocardiogram was repeated after continued oral losartan therapy 50 mg QD for 30 ± 13 days. The effects of losartan are tabulated below.

	Baseline	4 hours	P*	1 month	P*
MBP (mmHg)	107 ± 11	91 ± 11	< 0.0001	93 ± 7	0.0001
ERO (mm2)	43 ± 17	36 ± 16	< 0.0001	37 ± 18	< 0.0001
RVol (cc)	75 ± 29	64 ± 27	< 0.0001	69 ± 29	< 0.0001
EDVI (ml/m2)	128 ± 20	115 ± 18	< 0.0002	117 ± 16	0.0029
ESVI (ml/m2)	48 ± 26	42 ± 23	0.034	40 ± 20	0.14

* P-value for the comparison with baseline using a paired t-test.

Conclusions: We concluded that treatment of mitral regurgitation using the angiotensin II blocker losartan, 1) has favorable effects with a significant reduction of regurgitant volume, regurgitant orifice and left ventricular remodeling; 2) these favorable effects appear to persist with time, 3) are of moderate magnitude, suggesting that 4) the evaluation of the clinical effects of the medication in a controlled trial is warranted.

2:15

852-2 Long-term Therapy With Enalapril in Asymptomatic Patients With Moderate to Severe Chronic Mitral Regurgitation

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Background: Vasodilators acutely reduce regurgitant volume and improve left ventricular (LV) performance in mitral regurgitation (MR), but more data are necessary about their long-term efficacy.

Methods: To assess the long term effect of ACE inhibition in asymptomatic patients (pt) with moderate to severe MR we compared) echocardiographic left ventricular (LV) performance in 30 pt before and after 6 months. After randomisation 15 pt were allocated to enalapril (E) therapy (24 ± 7 mg/day) and 15 pt served as control (C).

Results: There were no differences in baseline Echo measurements of LV diameters, volumes, mass and mean wall stress (MWS) between E and C groups. After 6 months pt receiving E had a reduction in end-diastolic diameter (EDD) (from 63.9 ± 6.7 to 60.5 ± 4.1 mm, p = 0.02) and volume (EDVI) (from 115.9 ± 21.4 to 102.9 ± 13.6 ml/m^2, p = 0.02). LV mass (from 176.5 ± 41.0 to 151.4 ± 22.6 g/m^2, p < 0.02) and MWS (from 253.0 ± 36.1 to 223.6 ± 26.8 kdyne/cm^2, p < 0.01). End-systolic diameter (ESD), volume (ESVI) and EF were not altered. In C group EDD, ESD, EDVI, ESVI, EF, mass and MWS did not change significantly after 6 months. In addition, there was a clear difference between E and C group in EDD (60.5 ± 4.1 vs 65.3 ± 7.1 mm, p = 0.03), ESD (37.7 ± 4.1 vs 40.5 ± 4.2 mm, p = 0.07), EDVI (102.9 ± 13.6 vs 117.9 ± 28.2 ml/m^2, p < 0.05), mass (150.4 ± 22.6 vs 168.3 ± 29.5 g/m^2, p < 0.05) and MWS (223.6 ± 26.8 vs 257.3 ± 31.0 kdyne/cm^2, p < 0.01) after 6 months.

Conclusions: Long term therapy with enalapril in asymptomatic pt with moderate to severe chronic MR reduces LV size and mass suggesting the potential to delay timing for mitral valve surgery.

2:30

852-3 Beta Blockade Must be Added to ACE Inhibition to Improve Hemodynamics and Contractile Function in Experimental Mitral Regurgitation

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Although well established in the therapy of congestive heart failure, the role of ACE inhibitors and beta-blockers in mitral regurgitation (MR) remains controversial. Accordingly, we studied the sequential effects of lisinopril (L) and atenolol (A) (L + A) on 7 dogs with severe left ventricular (LV) dysfunction due to 3 months of MR.

	Baseline	3 mo MR	6 mo MR + L	9 mo MR + L + A
LV mass/BW (g/kg)	4.47 ± 0.25	5.81 ± 0.33	5.60 ± 0.43	6.13 ± 0.41*
RF (%)	60.0 ± 1.5	65.2 ± 4.1	62.4 ± 2.9	56.4 ± 4.7
PCW (mmHg)	9.6 ± 1.3	15.4 ± 1.7	12.1 ± 1.2	9.1 ± 1.4#
K index	3.48 ± 0.17	2.51 ± 0.15*	2.91 ± 0.16	3.35 ± 0.19#

*p < 0.05 vs baseline, #p < 0.05 vs 3 mo. BW = body weight, RF = regurgitant fraction, PCW = pulmonary capillary wedge pressure, K = end systolic stiffness.

We conclude that while there was a tendency for improvement in hemodynamics with L, only the combination of L + A improved hemodynamics and normalized contractility.

2:45

852-4 Effects of Inhaled Nitric Oxide in Patients With Severe Mitral Stenosis and Normal Left Ventricular Function

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Mitral stenosis is associated with increased left atrial pressure and pulmonary hypertension in the setting of normal left ventricular function. The hemodynamic effects of inhaled nitric oxide (NO), a selective pulmonary vasodilator, in mitral stenosis are unknown. Nine women (mean age 61 ± 7 years) with severe rheumatic mitral stenosis (mean valve area (MVA) of 1.1 ± 0.2 cm^2) and normal LV function underwent right and left (via transseptal approach) heart catheterization; measurements were made at baseline, and after inhaling NO (80 ppm) for 10 minutes (mean ± SD; * = p < 0.05).

	Baseline	Nitric Oxide
Ao mean (mmHg)	96 ± 11	96 ± 13
LVEDP (mmHg)	15 ± 4	15 ± 5
LA mean (mmHg)	26 ± 3	27 ± 5
PA Systolic (mmHg)	62 ± 13	54 ± 14*
CO (Fick, l/min)	4.2 ± 1.0	4.3 ± 1.2
SVR (Wood U)	22.1 ± 7.0	21.5 ± 6.8
PVR (Wood U)	3.5 ± 2.6	2.1 ± 1.4*

In 6 patients who underwent successful balloon valvuloplasty, MVA increased from 1.0 ± 0.1 to 1.6 ± 0.3 cm^2 with a decrease in LA pressure (26 ± 2 to 19 ± 4 mmHg, p < 0.05) and PA systolic pressure (55 ± 3 to 44 ± 7 mmHg, p < 0.05). The CO (4.3 ± 1.0 l/min to 4.2 l/min, p = NS) and PVR were unchanged (3.0 WU to 2.8 WU, p = NS).

Conclusions: 1) NO reduced PVR in patients with mitral stenosis and normal LV function by decreasing PA pressure without altering LA pressure or CO. This differs from previous findings in patients with LV dysfunction in whom NO reduced PVR solely by increasing pulmonary wedge pressure. 2) PVR was unchanged immediately after valvuloplasty, despite evidence that it is not fixed as shown by the vascular reactivity with NO. This suggests a need for chronic adaptation to the reduction in LA pressure.

3:00

852-5 Diastolic Function in the Progression From Acute to Chronic MR

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Background: The change in LV diastolic function during the progression from acute to chronic MR is unclear.

Methods: Fifteen dogs underwent placement of 20 LV myocardial markers. MR was created by puncturing the posterior leaflet with a Cope biopsy needle. Biplane videofluoroscopic studies, performed at 1 week (acute MR) and 3 months (chronic MR), were used to assess LV volume and wall stress. Diastolic function was assessed by the maximum time derivative and time constant of isovolumic pressure decay (τ; -dP/dt), time constant of