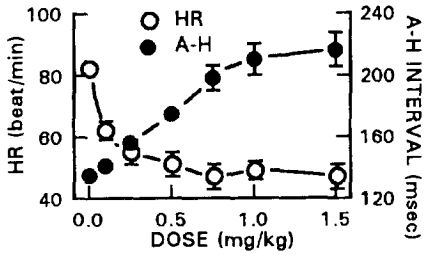
	HR	SNRTc	SACT (ms)	P-A (ms)	A-H (ms)	H-V (ms)	P (ms)	P-R (ms)	QRS (ms)	QTc (ms)	AERP (ms)	$VAPD_{90}$ (ms)
Ctrl	78	1.28	130	20	135	68	68	187	115	501	175	413
	±8	±0.2	±20	±2	±19	±8	±9	±12	±31	±33	±10	±16
Zat	43	2.27	140	20	178	70	70	235	122	553	260	562
	±9	±0.3	±29	±2	±24	±8	±9	±13	±32	±35	±14	±15
P	<0.01	<0.001	NS	NS	<0.01	NS	NS	<0.01	NS	<0.01	<0.01	<0.01
ED_{50} (mg/kg)	0.23	0.22	–	–	0.58	–	–	0.57	–	0.76	0.60	0.78

Conclusion: At low dose, Zat has a depressant effect on sinus nodal function; at higher doses, it has additional actions on A-V nodal function and lengthens repolarization reflecting effects on other ion channels.



799 Dilated Cardiomyopathy

Wednesday, March 22, 1995, 2:00 p.m.–3:30 p.m.
Ernest N. Morial Convention Center, Room 16

2:00

799-1 Gender-Related Differences in Functional and Morphologic Features in Idiopathic Dilated Cardiomyopathy

Francesco Pelliccia, Giulia d'Amati, Cinzia Cianfrocca, Stefano De Castro, Paola Bernucci, Pietro Gallo, Giuseppe Critelli. *Departments of Cardiology and Human Biopathology, University "La Sapienza", Rome, Italy*

Recent studies have shown that a paradox occurs in ischemic heart disease, as women (W) show a higher incidence of heart failure than men (M) despite similar LV ejection fractions. Aim of this study was to verify whether such a "gender paradox" also exists in idiopathic dilated cardiomyopathy (IDC) and, if so, which are the possible underlying factors. Accordingly, we analyzed the clinical, ECG, echocardiographic, hemodynamic and LV histomorphometric features of 75 IDC patients (48 M and 27 W), consecutively referred to our Unit for invasive evaluation. W were older (55 ± 9 vs 45 ± 11 yrs, $p < 0.005$), more symptomatic (NYHA class III or IV in 63 vs 35%, $p < 0.05$), and had more frequent signs of heart failure (70 vs 42%, $p < 0.04$), as compared with M. At echocardiography, the two groups had similar LV diameter, volume and mass. Doppler examination, however, showed that W had a lower ratio of transmitral early to late peak filling waves than M (1.0 ± 0.3 vs 1.4 ± 0.4, $p < 0.001$), thus indicating a worse LV diastolic filling dynamics. At catheterization, W showed higher mean pulmonary artery pressure (25 ± 9 vs 19 ± 8 mmHg, $p < 0.005$), and LV end-diastolic pressure (21 ± 7 vs 16 ± 8 mmHg, $p < 0.01$) than M, whereas LV ejection fraction and cardiac index were similar in both genders. Comparison of LV histomorphometric features did not show any difference in myocellular area, nuclear area, and myofibril volume fraction. Conversely, W had larger interstitial fibrosis (12 ± 6 vs 7 ± 5%, $p < 0.001$), and endocardial fibrosis (15 ± 5 vs 8 ± 6%, $p < 0.001$), as compared with M. It is concluded that: (1) the paradox observed in ischemic heart disease of more frequent symptoms and signs of heart failure in W than in M occurs also in IDC; (2) such "gender paradox" relates to differences between W and M in LV diastolic function, rather than in cardiac contractility; (3) the association of female gender with a larger accumulation of cardiac fibrous tissue seems to constitute the morphologic substrate of the phenomenon.

2:15

799-2 Left Ventricular (LV) and Myocyte Electrophysiology with the Development of Dilated Cardiomyopathy (DCM); Effects of Angiotensin II Receptor (AT_1 AT-II) Blockade

William S. McMahon, Rupak Mukherjee, Henry H. Holzgrefe, David S. Buckles, Paul C. Gillette, James R. Powell, William H. Koster, Francis G. Spinale *Med Univ of South Carolina, Chas, SC; Bristol Myers Squibb Research Institute, Princeton, NJ*

Ventricular arrhythmias are a significant cause of morbidity and mortality with DCM, and AT_1 AT-II receptor activation has been implicated to play a role in arrhythmogenesis. However, the effects of AT_1, AT-II receptor activation on changes in LV function and myocyte electrophysiology during the progression of DCM remain unexplored. Accordingly, this study measured weekly changes in LV function (ejection fraction, LVEF; peak systolic wall stress, LVWS) and surface electrocardiography (R-R interval, QRS duration, QTc interval), and myocyte action potentials (resting membrane, RM; upstroke velocity, Vmax; duration at 90% repolarization, APD_{90}) at terminal study in 3 groups of dogs (n = 6/group): DCM, chronic pace (216 bpm, 4 weeks); DCM/AT-BLOCK, chronic pace and treatment with a specific non-peptide AT_1 AT-II antagonist (SR 47436 (BMS 186295); 30 mg/kg BID); and control (CON). All measurements were made with the pacemaker deactivated.

	LVEF (%)	LVWS (g/cm^2)	R-R (ms).	QRS (ms).	QTc (ms)
Week 2:					
CON	68.7 ± 3.2	133 ± 14	646 ± 99	58.4 ± 1.3	291 ± 13
DCM	40.9 ± 4.1*	184 ± 16*	519 ± 40	60.7 ± 1.9	316 ± 9
DCM/AT-Block	44.1 ± 3.7*	138 ± 10+	540 ± 56	63.2 ± 1.2*	325 ± 9
Week 4:					
CON	73.1 ± 2.4	127 ± 10	629 ± 45	57.6 ± 1.4	314 ± 9
DCM	35.2 ± 3.5*	223 ± 16*	505 ± 41*	62.0 ± 1.9	313 ± 9
DCM/AT-Block	35.2 ± 2.7*	160 ± 13*+	578 ± 48	65.7 ± 1.5*	296 ± 6

*$p < 0.05$ vs CON, +$p < 0.05$ vs DCM

With DCM, RM (−71 ± 1* vs −78 ± 1 mV) and APD_{90} (257 ± 9* vs 226 ± 7 ms) increased, and Vmax decreased (121 ± 5* vs 158 ± 9V/s) compared to CON. In contrast, with AT-BLOCK, RM became more negative (−76 ± 1+ mV), APD_{90} was reduced (183 ± 14*+) and Vmax increased (165 ± 13+). *Summary:* AT_1 AT-II receptor blockade during the progression of DCM caused significant changes in LV myocardial conduction and myocyte action potentials. These results suggest that AT_1 AT-II receptor activation plays a contributory role toward the changes in LV electrophysiology with DCM.

2:30

799-3 Left Ventricular Function and Immunohistological Findings in Patients with Dilated Cardiomyopathy: A Follow-up Study

Igor Janda, Mira C. Schannwell, Otto N. Krogmann, Uwe Kühl, Heinz P. Schultheiss [1], Bodo E. Strauer. [1] *Dept. of Cardiology, Benjamin Franklin, Berlin; University of Düsseldorf, Germany*

Right ventricular endomyocardial biopsies and biplane left ventricular (LV) angiocardiography with high fidelity pressure measurements were performed in 32 patients (pts) with dilated cardiomyopathy. LV systolic function was assessed by the ejection fraction (ef; %). Parameters of LV diastolic function were: time constant of relaxation (T; ms), constant of myocardial stiffness (stress-strain relationship, b) and the relation of early to late peak filling rate (epfr/lpfr). Immunohistological evaluation revealed lymphocytic infiltration and increased expression of human leucocyte class I and II antigens (HLA) in 15 pts (P). At follow-up after 6 months myocardial inflammation resolved in 8 pts (FU). Ventricular function was compared to 17 pts with no inflammation (C). Systolic function was equally disturbed in all groups. Diastolic dysfunction was more pronounced in pts with myocardial inflammation and improved with resolvement of inflammation:

	EF	LMM	EDV	EDP	T	b	epfr/lpfr
C	33	141	166	16	113	28	1.39
P	35	148	173	24†	104	51†	1.70†
FU	33	141	166	16*	113	32*	1.39*

EF: ejection fraction, LMM: muscle mass index (g/m^2), EDV: end-diastolic volume index (ml/m^2), EDP: end-diastolic pressure (mmHg), *$p < 0.05$ vs. P. †$p < 0.05$ vs. C

Thus: Myocardial inflammation in patients with dilated cardiomyopathy causes a pronounced increase of diastolic myocardial stiffness. Spontaneous resolvement of inflammatory signs is parallaled by improvement of LV diastolic, but not systolic function.