997-87 ELISA Titres of Anti-α Myosin Antibodies in Idiopathic Dilated Cardiomyopathy Patients Reduce with Disease Progression

Jonathan H. Goldman, Rahat S. Warraich, Philip J. Keeling, Simon Redwood, L. Dalla Libera [1], Perry Elliott, Alida L.P. Caforio [1], William J. McKenna. *St. George's Hospital Medical School, UK; [1] Dept. Cardiology, University of Padua, Italy*

Immunofluorescence detects anti-heart antibodies directed against a range of cardiac antigens in 30% of patients with idiopathic dilated cardiomyopathy (DCM), but is not antigen specific. Western blots showed that these antibodies recognise both α (organ specific, atrial) and β (cross reactive ventricular and skeletal) myosin but this technique is nonquantitative and unsuitable for screening purposes. To assess the frequency and titre of the anti-a myosin antibodies, we developed a biotin-streptavidin ELISA for detection of IgG to purified human atrial myosin. A pilot study of 40 DCM patients and 40 IHD controls revealed 94% concordance between ELISA and Western Blot. Studies were performed on sera (dilution 1/320) from 123 consecutive patients with DCM (WHO criteria) presenting to our hospital (age 42 ± 14). These were compared with sera from 52 normals (45 ± 16) and 58 patients with ischaemic heart disease (IHD) (65 ± 12), (40% had poor LV function, 65% had previous MI). Raised antibody levels to atrial myosin were found in 24 (20%) of DCM patients, 1 (2%) normal control and 3 (5%) of the IHD patients (DCM v. IHD $p < 0.05$, IHD v. normal $p = 0.4$). Mean antibody level ± SEM in DCM patients were greater than IHD patients (0.27 ± 0.02 v. 0.20 ± 0.01; $p = 0.001$) but IHD did not differ from normals (0.20 ± 0.01 v. 0.18 ± 0.01; $p > 0.1$). Repeat evaluation on 57 DCM patients after 20 ± 20 months showed significant reduction in antibody level from 0.3 ± 0.02 to 0.23 ± 0.01 ($p = 0.04$). In conclusion we confirm the presence of disease specific anti-α myosin antibodies in DCM patients and show a reduction in antibody level over time as in other autoimmune diseases.

997-88 Ventricular Remodeling During Pacing Induced Congestive Heart Failure: The Logarithmic Model of Passive Properties is Physiologically and Mathematically Superior to the Exponential Model!

Edward Yellin, Steven Solomon, William Stevenson-Smith, Srdjan Nikolic. *Albert Einstein College of Medicine, The Bronx, NY*

Ventricular remodeling is an important adaptation to both physiologic and pathologic stress and is accompanied by changes in passive myocardial and chamber properties. The analysis of remodeling and its subsequent effect on the dynamics of both systolic and diastolic function, requires the use of an appropriate mathematical characterization. We compared the exponential and logarithmic models in a study of ventricular dilatation following four weeks of rapid ventricular pacing (240/min) in dogs. We start by rejecting the relation, $P = Ae^{kV}$, because it does not allow for a positive value of the equilibrium volume, V_o, ie, the volume at zero transmural pressure, and we use: $P = P_\infty[e^{k(V-Vo)} - 1]$, so that stiffness is given by: $dP/dV = k(P + P_\infty)$. Thus, *both* k and P_∞ (the pressure asymptote) determine chamber stiffness. It is important to note the mathematical limitations of an exponential: because P_∞ is small and because the equation is asymptotic to the volume axis, there is a strong tendency to underestimate V_o, often giving negative values when using nonlinear regression analyses. These mathematical and physiological problems are overcome by the logarithmic model: $P = -S_p\ln[(V_m - V)/(V_m - V_o)]$; $dP/dV = S_p/(V_m - V)$, where S_p is a stiffness parameter in the positive plane, and V_m is the maximum physiologic volume that the ventricle can tolerate. V_o, an important parameter in remodeling, is accurately determined because the equation is not asymptotic to the volume axis. Furthermore, S_p has the units of stress and thus characterizes the myocardium, and, when normalized by the operating volume, $V_m - V_o$, the chamber.

	S_p (mmHg)	V_m (ml)	V_o (ml)	P_∞ (mmHg)	α (l/ml)
C	9 ± 4	80 ± 15	39 ± 11	7 ± 3	0.03 ± 0.01
HF	6 ± 2	159 ± 31	97 ± 15	2 ± 1	0.04 ± 0.02
p>	0.03	0.0001	0.0001	0.0001	NS

Thus, in this model of heart failure, chronic depression of contractility requires constant use of the Frank-Starling mechanism to maintain cardiac output, and the ventricle remodels by dilating (both V_m and V_o increased) as well as by *increasing* compliance (S_p decreased). This growth pattern is adaptive, although it may not allow regression. The exponential model failed to show a change in stiffness. The logarithmic approach is both physiologically and mathematically superior.

997-89 Effect of Local Angiotensin II Inhibition on Pattern of Ventricular Hypertrophy and Characteristics of Myocardium

Masakazu Obayashi, Michihiro Kohno, Masahumi Yano, Shigeki Kobayashi, Tsutomu Ryouke, Tomoko Ohkusa, Masunori Matsuzaki. *Yamaguchi University School of Medicine, Ube, Japan*

The purpose of this study was to examine the effect of local angiotensin II (ATII) inhibition on amount and pattern of pressure overload-induced ventricular hypertrophy and functional characteristics of myocardium. We administered abdominal aorta-constricted rats vehicle (C), 0.3 mg/kg/day (low dose; LD), and 3.0 mg/kg/day (high dose;HD) of ATII receptor antagonist TCV-116. After 4 weeks treatment, we measured LV pressure using micromanometer and wall thickness using 20 MHz ultrasonic wall tracker for calculating LV dimension (D) and midwall fiber stress (FS).

	C (n = 7)	LD (n = 9)	HD (n = 10)
Peak LVP (mmHg)	165 ± 10	141 ± 9*	137 ± 12*
LV weight (mg/gBW)	2.89 ± 0.03	2.40 ± 0.26*	2.05 ± 0.20*#
end-diastolic WT (mm)	3.7 ± 0.2	3.0 ± 0.3*	3.0 ± 0.2*
end-diastolic D(mm)	3.8 ± 0.6	4.6 ± 0.7*	3.9 ± 0.5#
cell width (μ m)	16.3 ± 0.6	13.6 ± 0.3*	13.4 ± 0.6*
peak FS ($\times 10^3$dyn/cm^2)	80 ± 8	86 ± 17	69 ± 8#
k	−4.9	−4.9	−8.5

*$p < 0.01$ vs C, #$p < 0.01$ vs LD k; the slope of regression line between %shortening of LVD (Y-axis) and peak FS (X-axis)

In LD of TCV-116, WT and cell width significantly decreased compared with C in spite of the tendency to increase in peak FS. On the other hand, HD of TCV-116 could inhibit not only development of cell width but also LV dilatation, accompanied with significant reduction of FS. Peak(+)dP/dt of LVP and heart rate did not change between LD and HD. The slope (k) was higher in HD considered as concentric remodeling than in LD as inadequate eccentric remodeling. These results suggest that change in LV geometry and functional characteristics of myocardium could depend on the degree of blocking action of local ATII.

997-90 Right (RV) and Left Ventricular (LV) Geometry and Myocyte Contractile Processes with Dilated Cardiomyopathy (DCM): Disparity Between Myocyte Growth and β-Adrenergic Responsiveness

William S. McMahon, Paul C. Gillette, Fred A. Crawford, Francis G. Spinale. *Med Univ of South Carolina, Charleston, SC*

The progression of DCM has been assumed to be a homogenous process for both the RV and LV. However, this assumption has never been tested. Accordingly, we measured myocyte contractile performance (velocity of shortening, VELSHORT; percent shortening, PERSHORT) at baseline (BASE) and after β-adrenergic receptor stimulation (βAR, 25 nM isoproterenol) of isolated myocytes taken from the RV and LV of 5 pigs with pacing induced DCM (240 bpm, 3 weeks) and 5 control pigs (CON). RV and LV mass/body weight (MASS) and myocyte length and cross-sectional area (CSA) were also determined.

	CON-RV	CON-LV	DCM-RV	DCM-LV
VELSHORT-BASE (μm/s)	90 ± 5+	50 ± 1	48 ± 2*+	32 ± 1*
VELSHORT-βAR (μm/s)	206 ± 8+	150 ± 5	123 ± 8*	111 ± 9*
PERSHORT-BASE (%)	5.8 ± 0.2+	4.6 ± 0.1	3.1 ± 0.1*+	2.2 ± 0.1*
PERSHORT-βAR (%)	11.5 ± 0.3+	10.2 ± 0.3	5.9 ± 0.3*	5.2 ± 0.4*
Length (μm)	150 ± 2+	137 ± 1	179 ± 2*+	173 ± 2*
CSA (μm^2)	176 ± 4+	362 ± 8	232 ± 4*+	292 ± 5*
Mass (gm/kg)	0.8 ± 0.1+	2.8 ± 0.1	1.6 ± 0.1*+	2.9 ± 0.2

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

In controls, RV myocytes were longer and had a smaller CSA, but enhanced contractile performance at baseline and with β-adrenergic stimulation. With DCM, no LV hypertrophy occurred. In contrast, RV chamber and cellular hypertrophy occurred and was associated with a persistent increase of RV myocyte baseline contractile function. *Summary:* This study demonstrated, for the first time, that differences in RV and LV myocyte function and β- adrenergic responsiveness exist in normal and DCM states. More importantly, a disparity in RV and LV myocyte growth with DCM occurred. Thus, in this model of DCM, RV and LV growth and changes in contractile performance are not a homogenous process, and suggest that inherent differences exist in the response of RV and LV myocytes to stress.