	Basal	Pravastatin	% var.	p <
TCH	282 ± 55	224 ± 50	−23	0.001
LDL	195 ± 46	133 ± 45	−32	0.001
WT	3.4 ± 0.5	2.8 ± 0.4	−18	0.001
WT/r	0.36 ± 0.08	0.29 ± 0.08	−19	0.001
C-WT	1.73 ± 0.21	1.48 ± 0.15	−14	0.01
C-IMT	0.86 ± 0.15	0.62 ± 0.12	−28	0.001
C-MWT	0.87 ± 0.08	0.86 ± 0.07	−1	NS

It's concluded that pravastatin reducing TCH and LDL plasma levels in dyslipidemic pts, decreases AA- and C-WT; this is due to the decreased thickness of intima-media layer (IMT) of the wall, whereas MWT is unmodified.

1014 Heart Failure: Cellular Mechanisms and Adaptation

Wednesday, March 22, 1995, Noon–2:00 p.m.
Ernest N. Morial Convention Center, Hall E
Presentation Hour: 1:00 p.m.–2:00 p.m.

1014-92 Impaired Microcirculation in Chronic Heart Failure

Daniel Duprez, Eric Dhondt, Marc De Buyzere, Denis Clement. *University Hospital, Gent, Belgium*

The microcirculation plays a crucial role in the exchange of oxygen, energy rich substrates and metabolites. The effects on the microcirculation of impaired heart function and disturbed peripheral skin circulation in chronic heart failure (CHF) are unknown. Nailfold capillary morphology and dynamics in CHF were studied in relation to parameters of left ventricular (LV) structure and function. Twenty patients (13 male, 7 female, age 64 ± 2 years) with CHF NYHA class II underwent a capillaroscopic examination at the finger nailfold using a computerised videophotometric system (Capiflow) at rest and after 1 min arterial occlusion. Patients were treated with diuretics, ACE inhibitors and digoxin and mean duration of symptoms was 65 ± 9 months. Study parameters were number, length, and diameter of the capillaries as well as capillary blood velocity (CBV). Further experiments included echocardiography and determination of LV ejection fraction by Tc-scintigraphy. Nailfold capillaries in established CHF are enlarged (afferent diameter 6.6 ± 0.4 μm, efferent diameter 8.2 ± 0.4 μm, ref. resp. < 6 and < 8 μm) and CBV is dramatically decreased (351 ± 64 μ/s, ref. > 600 μm/s at 23°C). The reactive hyperemic response to one minute arterial occlusion is attenuated (peak CBV 879 ± 158 μm/s, ref > 2000 μm/s). CBV correlates positively with LV ejection fraction ($r = 0.61$, $p = 0.01$) and inversely with LV end-diastolic ($r = -0.56$, $p = 0.04$) and end-systolic ($r = -0.69$, $p = 0.01$) diameters. The time-to-peak flow (35 ± 5 s, ref. 6–10 s) after one min arterial occlusion is positively related ($r = 0.68$, $p < 0.05$) to the duration of CHF. Our data indicate that microcirculation in chronic heart failure deteriorates in function of the severity and duration of heart failure.

1014-93 Impaired Endothelium-Dependent Dilation of Resistance Arteries in Congestive Heart Failure (CHF)

Kiyomitsu Ikeoka, Tooru Arii, Keiko Takahashi, Suguru Kobayashi, Mitsumasa Ohyanagi, Tadaaki Iwasaki. *Hyogo College of Medicine, Nishinomiya, Japan*

Patients with CHF have abnormal endothelium-dependent vasodilator response to acetylcholine (ACh). The purpose of this study was to determine whether the impaired endothelium-dependent dilation of peripheral resistance arteries in CHF is related to a specific defect of the endothelial cell muscarinic receptor or to a more generalized abnormality of the vascular endothelium. Arterioles (mean diameter 89 ± 10 μm) obtained from the cremaster muscle of Wistar rats (n = 29) were double-cannulated with glass micropipets and pressurized (65 mmHg), and dilator responses were studied using in vitro video microscopy. CHF was produced by the occlusion of left coronary arteries of rat's hearts. Rats were sacrificed at 2 or 8 weeks after CHF was created (LVEDP 20 ± 3 and 23 ± 4 mmHg, respectively). Vasomotor responses to ACh were significantly blunted in both CHF groups (ED50 5.8 ± 0.4, 5.5 ± 0.6 vs. 6.9 ± 0.3 in control, $p < 0.05$). Vasodilator responses to bradykinin, calcium ionophore A23187 were similar in 2ws-CHF and control, however, reduced in 8ws-CHF. ED50 of bradykinin in 8ws-CHF and control were 7.1 ± 0.5 and 8.3 ± 0.4 ($p < 0.05$), and those of A23187 were 6.5 ± 0.3 and 7.6 ± 0.3 ($p < 0.05$), respectively. The responses to nitroprusside were not significantly different among three groups. These findings indicate that the abnormality exists in transmembrane signal transduction including Gi coupling in the early phase of CHF and progress to the final stage of nitric oxide synthesis in chronic CHF.

1014-94 Activated Endothelial and Interstitial Cells in Chronic Myocarditis — Expression of Endothelial Adhesion Molecules

Michel Noutsias, Uwe Kühl, Heinz-P. Schultheiß. *Benjamin-Franklin-Hospital, FU Berlin, F.R. Germany*

A chronic immunological process — based on an initial event of myocarditis, probably triggered by a viral infection — is considered as a possible pathogenetic mechanism for dilated cardiomyopathy (DCM). The cytokine-respondent induction of adhesion molecules on endothelial cells (EC) enables the adhesion of immunocompetent cells to activated EC and the consecutive transmigration. We studied the expression pattern of adhesion molecules (immunoglobulin-superfamily and β_1-integrins) in biopsies from patients with clinically suspected DCM (n = 134). Immunohistologically negative specimens (n = 61: poor lymphocytic infiltration) presented a missing or weak immunoreactivity of adhesion molecules on EC. An enhanced intensity of expression was noticed in the percentage of positive biopsies (n = 73: pathologically increased lymphocytic infiltration >2.0 CD 3-lymphocytes per high power field/HPF, x400-fold magnification) depicted at the following table:

	Negative (n = 61)		Positive (n = 73)	
Antigen	Endothel	Interstitium	Endothel	Interstitium
HLA class I	15%	13%	63%	68%
HLA DR	20%	18%	55%	64%
ICAM-1/CD 54	25%	11%	84%	77%
VCAM-1	23%	–	88%	–
VLA-β/CD 29	26%	26%	89%	70%
VLA-4/CDw49d	15%	13%	66%	37%
LFA-3/CD 58	18%	16%	66%	36%

Conclusions: Pathologically increased lymphocytic infiltrates in chronic myocarditis are associated with an endothelial and interstitial inflammatory activation. This phenomenon is independent of focally concentrated infiltrates. Thus, the implication of adhesion molecules in the immunohistological diagnosis of myocarditis could provide further information apart from the sole criterion "lymphocytic infiltration" and minimize the "sampling-error-effect".

1014-95 Comparative Effect of Inotropic Agents on Oxygen Expenditure Between β-Stimulation, Phospho-Diesterase Inhibition and Ca^{2+} Sensitization

Hideyuki Takaoka, Motoshi Takeuchi, Katsuya Hata, Masuki Mori, Hideyuki Yamakawa, Kozo Yamaguchi, Mitsuhiro Yokoyama. *Kobe University School of Medicine, Kobe, Japan*

A newly developed cardiotonic agent, MCI-154, increases sensitivity of myofilament to Ca^{2+}, which could generate force with less Ca^{2+}, and hence potentially save myocardial oxygen consumption (VO_2). We compared the effect of MCI-154 (MCI; 16.6 μg/min, n = 12) on VO_2 to those of dobutamine (Dob; 5 mu;g/kg/min, n = 12) and phospho-diesterase inhibitor, E1020, (PDE-I; 0.3 μg/kg/min, n = 10) in patients with left ventricular (LV) dysfunction. Inotropic and vasodilative actions were assessed by LV elastance, E_{max}, and effective arterial elastance, E_a, by the conductance catheter, and VO_2 by the Webster catheter. Total mechanical energy was assessed by the systolic pressure-volume area (PVA) consisting of external work (EW) and potential energy (PE). VO_2 ($VO_{2,total}$) was divided into PVA-dependent component ($VO_{2,EW}$ and $VO_{2,PE}$) and PVA-independent component ($VO_{2,NMW}$) used for non-mechanical work (excitation-contraction coupling or Ca^{2+} handling). *Results:* Increases in E_{max} was comparable (Dob; 42 ± 21, PDE-I; 44 ± 13, MCI; 56 ± 34%, ns) but decline in E_a was the largest with PDE-I (Dob; 9 ± 37, PDE-I; −19 ± 13#, MCI; 1 ± 14%, $p < 0.05$ by ANOVA).

	$\Delta VO_{2,total}$	$\Delta VO_{2,EW}$	$\Delta VO_{2,PE}$	$\Delta VO_{2,NMW}$
Dob	1.1 ± 0.8*	0.56 ± 0.64*	−0.3 ± 0.6	0.8 ± 0.8*
PDE-I	−0.1 ± 0.7	0.12 ± 0.21*	−0.9 ± 1.2*	0.7 ± 1.2*
MCI	−0.5 ± 0.9*	0.08 ± 0.37	−0.7 ± 0.7*	0.1 ± 0.4

mean ± SD in J/beat, *p < 0.05 vs corresponding control

Dob increased $VO_{2,total}$ but MCI remained unchanged $VO_{2,total}$ mainly due to the decline in $VO_{2,PE}$. Unlike Dob and PDE-I, MCI did not increase $VO_{2,NMW}$, leading to the decreases in $VO_{2,total}$, which may result from less VO_2 for non-mechanical work. In conclusion, Ca^{2+} sensitizer, MCI-154, saves oxygen expenditure for non-mechanical work different from β-stimulant and PDE inhibitor.