Monday, March 4, 1991
10:30AM–12:00NOON, Room 257, West Concourse
Mechanisms of Myocardial Dysfunction: New Insights

10:30

VENTRICULAR RELAXATION AND MYOCARDIAL ISCHEMIA: A COMPARISON OF DIFFERENT MODELS OF TAU

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Prolonged myocardial relaxation is an early and sensitive indicator of myocardial ischemia and has been characterized by the time constant, tau. However, there is no consensus about the sensitivity in detecting ischemia and variability of the different mathematical models used for the calculation of tau . To examine this, LV micromanometer pressure recordings were obtained in 10 pts undergoing coronary balloon angioplasty. All pts had normal resting global and regional wall motion. Hemodynamic measurements were obtained at baseline, 30 and 60 s during balloon inflation, and 60 s after deflation. With balloon inflation, LV dP/dt decreased significantly ($p<0.005$). Two semilogarithmic models of tau assuming a zero asymptote of LV pressure decline were measured. The first was obtained from data throughout isovolumic relaxation (T_L) while the other included only the first 40 ms after peak negative dP/dt (T_{40}). Two models assuming non-zero asymptotes were also measured: an iterative exponential model (T_E), and a derivative model (T_D). The first three models were also compared by their predicted time for LV pressure at peak negative dP/dt to decline by one half ($T_{1/2}$). Tau measurements (ms) were:

Time	T_L	$T_{1/2}$	T_{40}	$T_{1/2}$	T_E	$T_{1/2}$	T_D
Baseline	48	33	48	33	39	33	46
30 s	61*	42*	60*	41*	50**	43*	50
60 s	66*	46*	67*	46*	50	48*	48
Deflation	51	36	51	35	41	36	44

*$p<0.005$, **$p<0.05$ versus baseline (paired data)

Beat to beat variability (coefficient of variation) was least for T_L (5.9%) and T_{40} (4.8%) and greatest for T_E (23.0%) and T_D (22.4%). **Conclusions:** All models except T_D are sensitive to ischemia. However, $T_{1/2}$ derived from T_L or T_{40} may be more practical to use in terms of consistency between models and sensitivity to ischemia.

10:45

IONTOPHORETIC DELIVERY OF DOBUTAMINE : AN EFFECTIVE METHOD TO INCREASE CONTRACTILITY OF NON-TRANSMURAL INFARCTS

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Direct delivery of an inotropic agent to failing cardiac tissue will increase the efficacy of the drug and avoid its systemic effect. To achieve this goal, a cardioverter defibrillator electrode patch was modified to contain a 3 cc replenishable chamber lined with permeable membrane through which 1 mA/cm^2 80 msec pulsed electrical current synchronized with the ventricular depolarization was applied. Iontophoresis (IONTO) uses electrical current to transport charged molecules directly into tissues. The proximal LAD was occluded in 8 dogs for 30 days resulting in a histologically proven non-transmural patchy infarct. Dobutamine (DOB) 0.5 mg/cc was circulated through the chamber which was applied to the epicardial surface of the infarcted area for 10 min. IONTO delivery was compared to passive diffusion (PASS), using the same chamber and concentrations, and 10 min of IV administration of DOB at a concentration of 4 μgm/kg/min. Measurements were taken at 10 min during and 10 min post DOB application using epicardial echocardiography (5 MHz probe). Data = % change in wall thickness from control.

	IV	IONTO	PASS
During DOB	17±92	150±120	13±67
	NS	NS	NS
Post DOB	-35±18*	150±109	*-18±67

X±SD, *$p<0.05$ vs. IONTO.

Conclusion: Iontophoretic delivery of DOB into non-transmural infarcts results in a greater increase in contractility which persists for a longer period of time than either IV or PASS delivery. The goal of this work is to develop an iontophoretic delivery system which can be replenished transcutaneously, and will be programmed to deliver inotropic agents in titratable concentrations directly into failing myocardium.

11:00

VISCOSITY:COMPLIANCE RATIO - A NEW NONINVASIVE AGE-SENSITIVE INDEX OF ARTERIAL VISCOELASTICITY

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The impact of age-related changes in arterial stiffness on ventricular-vascular function cannot be assessed until arterial viscoelastic (VE) properties [i.e. arterial chamber compliance (C) and arterial wall viscous resistance (V)] are quantitatively evaluated. Until recently, values for these properties could only be acquired by invasive techniques. Thus, population studies to quantitate normal values for VE properties have not been performed. Recently validated noninvasive (NI) techniques were used to develop a viscoelastic index (VEI) which incorporates both C and V. VEI was defined as the ratio of V/C. C and V were determined from NI measurements of instantaneous aortic pressure (calibrated subclavian pulse tracings) and flow (echo-Doppler) in 76 normotensive subjects aged 20-81 years. Using a 3-element model of the arterial system, values for C and V were computed by an iterative procedure designed to minimize the absolute mean difference (D) between measured and "model" pressure waveforms. D was <8 mmHg in all subjects (mean 4±2(±SD) mmHg), reflecting the high precision of the vascular model used in this study. Below are the normal values for VEI (mean±SD):

n	18	17	15	14	9	3
Age (yrs)	20-29	30-39	40-49	50-59	60-69	>70
VEIx10^{-3}	68±20	70±25	77±22	79±27	118±40	133±29

Significant linear correlation was found between VEI and age ($r=0.54$, $p<0.001$). This age-VEI relation can be used as a reference for assessment of VE properties in patho-physiologic states. The VEI is a measure of the arterial VE contribution to ventricular-vascular function.

11:30

LEFT VENTRICULAR RELAXATION AND REGIONAL NONUNIFORMITY OF EARLY DIASTOLIC GEOMETRIC CHANGES IN HYPERTROPHIC NONOBSTRUCTIVE CARDIOMYOPATHY

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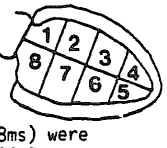
To study the relation between LV relaxation and early diastolic regional geometric changes, left ventriculography was conducted simultaneously with LV pressure micromanometry in 10 normal controls(C) and 11 Pts with hypertrophic nonobstructive cardiomyopathy(HCM). LV silhouettes in the right anterior oblique projection were divided into 8 areas(Figure) and regional wall stress (S; Janz's method) during isovolumic relaxation (IR) was determined. In HCM, both the IR time(IRT, 84±13ms) and the time constant of LV pressure fall(Tp,51±8ms) were significantly greater than in C(66±3ms, 36±5ms, respectively; $p<.01$), indicating impaired LV relaxation in HCM. End-systolic S was lower and the time constant of stress fall(Ts) was greater for each region in HCM than in C.



Area	2	3	4	5	6	7	
Ts C	38± 5	38± 6	40± 9	40±10	37± 5	35± 5	(ms)
HCM	57±12a	58±14a	63±20b	53±11b	54±11a	57±12a	

(a=$p<.01$ and b=$p<.05$ between C and HCM)

The coefficient of variation (CV) for Ts values in 6 areas of LV was calculated in each subject. This CV was greater in HCM than in C(13±7 vs 7±3%, $p<.05$), indicating regional nonuniformity in Ts. The CV was correlated with Tp ($r=.80$, $p<.01$) and IRT ($r=.79$, $p<.01$) in HCM. Thus, in HCM one of the causes of impaired global LV relaxation appears to be the regional nonuniformity of early diastolic geometric changes.