5.5 msec. The incidence of reentry was 0.018 ± 0.048 rotations/sec-cm^2. Of the 18 runs of VF in dogs with ablated ventricles, 8 episodes of reentry were detected. The mean lifespan was 3.6 ± 1.1 rotations ($p = 0.39$ compared with intact ventricles). The mean cycle length was 107.2 ± 9.6 msec ($p = 0.16$). The incidence of reentry was 0.075 ± 0.097 rotations/sec-cm^2 ($p = 0.048$). In both groups of dogs, dynamic displays of the activation patterns demonstrate that the reentrant wavefronts spiral rather than follow a simple circular pathway. *Conclusions:* (a) reentrant wavefronts are consistently present during Wiggers' stage II VF, (b) ablation of the subendocardium and Purkinje fibers results in an increased incidence of reentrant wavefronts on the epicardium, and (c) the reentrant wavefronts are compatible with spiral waves of excitation.

4:45

808-4 The Presence and Duration of an Excitable Gap During Ventricular Fibrillation in a Canine Model of Myocardial Infarction

George Horvath, Nikhil Patel, Roger S. Damle, Sandeep Jain, Nikki S. Robinson, Jeffrey J. Goldberger, Alan H. Kadish. *Northwestern University Medical School, Chicago, IL*

An excitable gap (EG) occupying 50% of the cycle length has been reported in a non-infarcted canine model of ventricular fibrillation (VF). To evaluate the presence and duration of an EG in VF post infarction, we studied 9 mongrel dogs at 5 days (n = 5) and 8 weeks (n = 4) post LAD ligation. VF induced by programmed stimulation was recorded using an 8 by 14 electrode array (2.5 mm interelectrode distance) over the infarcted area. The mean VF cycle length (VFCL) was determined at each site. EG was determined by a wavefront analysis propagation method. Sites at which both conduction and block occurred on different cycles were analyzed. At each, the interval from each activation to the subsequent blocked (R-B) or conducted (R-C) impulse was recorded, along with the R-C interval immediately preceding. The recovery period at each site was estimated as the range bounded by the maximal R-B and minimal R-C. The EG was determined by the difference of the recovery period and the mean R-C at each site. *Results:* Fifty eight sites were suitable for analysis.

Results of analysis (Mean or mean ± standard deviation):

Group	Mean R–C	Max R–B	Min R–C	EG	Mean EG as %CL
5 Day	154 ± 29 ms	104 ± 31 ms	124 ± 35 ms	29–49 ms	22–31%
8 Week	132 ± 23 ms	97 ± 21 ms	101 ± 25 ms	30–35 ms	23–30%
	$p = 0.002$	$p = 0.28$	$p = 0.008$		

The mean R-C at these sites was longer than the mean VFCL for all sites in the 5 day group (mean VFCL 133 ± 22 ms at 5 days, 130 ± 15 ms at 8 weeks). A trend toward a longer upper limit of EG was seen in the 5 day group ($p = 0.08$). In 29% of all sites (36% at 5 days, 20% at 8 weeks) a significant EG (≥10 ms) was not present.

Conclusions: An excitable gap exists at most sites during VF in a canine model of myocardial infarction, but is absent in a minority of sites. The gap may be shorter in absolute duration in chronic infarction (8 weeks) than in subacute infarction (5 days), although the proportion of cycle length occupied by the EG is similar in both groups. The site to site heterogeneity in the magnitude and presence of EG in infarcted myocardium has implications for the use of pacing techniques to modulate VF.

809 Autonomic Nervous System Adaptation in Heart Failure

Wednesday, March 22, 1995, 4:00 p.m.–5:00 p.m.
Ernest N. Morial Convention Center, Room 6

4:00

809-1 Different Respiratory Rates Affect the Measurement of Autonomic Tone by Power Spectral Analysis of Heart Rate Variability in Patients with Heart Failure

John E. Sanderson, Dickens T.K. Yeung, Leata Y.C. Yeung, Richard L.C. Kay, Brian Tomlinson, Luciano Bernardi [1], Kam S. Woo. *Chinese University of Hong Kong;* [1] *University of Pavia, Italy*

Power spectral analysis of heart rate variability is frequently used as an easy non invasive method for assessing autonomic tone. However changes in respiratory rate are frequently ignored and these may have an important effect on the measurements of spectral components, especially in heart failure. We have assessed the effect of different respiratory rates (10, 15, 20 min^{-1} and spontaneous) on low frequency (LF) and high frequency (HF) components of HR variability in 11 heart failure pts (CCF) (EF = 40 ± 4%; 9 males) and 9 normal subjects (5 males).

Results: LF & HF spectral power in normalized units (%); S = spontaneous (mean ± SEM)

	LF10	HF10	LF15	HF15	LF20	HF20	LFS	HFS
Supine								
CCF	19 ± 8	63 ± 9*	18 ± 5	54 ± 7	13 ± 4	47 ± 8*	16 ± 6	49 ± 8
Normal	14 ± 6	68 ± 8	18 ± 6	58 ± 10	15 ± 6	70 ± 5	22 ± 9	55 ± 10
Stand								
CCF	15 ± 7	66 ± 6	19 ± 7	46 ± 8	30 ± 10	51 ± 9	7 ± 5	31 ± 10
Normal	28 ± 9	55 ± 8	30 ± 9	42 ± 9	58 ± 10	27 ± 5	50 ± 12	17 ± 5

*$p < 0.05$

Supine HF power falls with increasing respiratory rate in most CCF pts and this effect is similar to that seen in normals on standing (i.e. at increased sympathetic levels). An improvement in clinical state of CCF pts will lower respiratory rate and this effect alone will increase HF power rather than any therapy.

4:15

809-2 Effect of Digoxin on Cardiac Sympathetic Activity in Congestive Heart Failure

Gary E. Newton, Jeffrey H. Tong, Anne M. Schofield, Andrew D. Baines, John S. Floras, John D. Parker *Mount Sinai Hospital, Toronto, Canada*

The effect of cardiac glycosides on cardiac sympathetic activity in congestive heart failure (CHF) remains uncertain.

Methods: We measured total body and cardiac norepinephrine spillover (NESP) using the norepinephrine isotope-dilution technique at baseline and 30 minutes after digoxin (0.25 mg iv). LV pressure, its first derivative (Millar), and systemic BP were also measured before and after digoxin. We studied 15 patients with CHF; 5 with normal LV filling pressures (LVEDP ≤ 14, mean 9 ± 2 mmHg), and 10 with high LV filling pressures (LVEDP > 14, mean 26 ± 3 mmHg).

Results: The groups had similar baseline HR, BP, and LV +dP/dt. The high LVEDP group had a lower EF (20 ± 2 vs 34 ± 2%, $p < 0.05$), a lower CI (1.7 ± 0.2 vs 2.8 ± 0.3 L/min/m^2, $p < 0.05$), and higher mean PA pressures (31 ± 4 vs 14 ± 2 mmHg, $p < 0.05$) at baseline, as compared to the normal LVEDP group. HR, BP, LVEDP, LV +dp/dt, coronary sinus blood flow, and total body NESP did not change in either group following digoxin. Cardiac NESP was unchanged in response to digoxin in the normal LVEDP group. Importantly, digoxin caused a consistent reduction in cardiac NESP in the high LVEDP group:

LVEDP	Cardiac NESP (pmol/min)	
	Baseline	Digoxin
≤14 mmHg	91 ± 28	111 ± 36
>14 mmHg	189 ± 63	159 ± 57*

All data expressed as mean ± SEM. *$p = 0.016$, by paired t test

Conclusion: This study demonstrates that the acute administration of digoxin reduces cardiac NESP in patients with CHF and high LV filling pressures. This reduction in cardiac sympathetic activity appears to be mediated by a non-hemodynamic mechanism, since digoxin in the dose used in this study did not cause changes in either the loading conditions or the contractile state of the LV.

4:30

809-3 Desipramine Attenuates the Cardiac Sympathetic Nerve Terminal Abnormalities in Congestive Heart Failure

Akito Yatani, Suzanne Y. Felten, Yoshihiro Himura, Michihiro Kashiki, Chang-seng Liang *University of Rochester Med. Ctr., Rochester, NY*

We have shown that cardiac norepinephrine (NE) reuptake activity and tyrosine hydroxylase (TH), a rate-limiting enzyme for NE synthesis, are reduced in congestive heart failure (CHF). To determine whether the changes of TH are caused by neurotoxic effects of NE, we administered the neuronal uptake inhibitor desipramine (DMI, 225 mg/day) to pacing-induced CHF and sham-operated (SHAM) dogs for 6 weeks. CHF was characterized by tachycardia, low aortic pressure, elevated left atrial pressure, decreased left ventricular dP/dt and reduced cardiac output. DMI produced no hemodynamic effects. The effects of DMI on left ventricular NE uptake activity (fmol/mg/15 min) and immunocytochemical TH profiles were:

Group	NE uptake	TH
SHAM (n = 12)	133 ± 9	813 ± 43
SHAM + DMI (n = 6)	49 ± 11*	769 ± 14
CHF (n = 12)	64 ± 8*	409 ± 42*
CHF + DMI (n = 7)	40 ± 9*†	642 ± 49*†

Values are mean ± SE. *$p < 0.05$ vs. SHAM; †$p < 0.05$ vs. CHF