Heart Rate Variability in Heart Failure and Sudden Death

Phyllis K. Stein, PhD

Washington University School of Medicine

St. Louis, MO

Washington University in St. Louis
School of Medicine

Outline

- Effect of erratic rhythm and sinus bigemeny on HRV.
- Traditional, non-linear HRV and heart rate turbulence and outcome in CHF.
- Traditional, non-linear HRV and heart rate turbulence and sudden death.

Erratic Rhythm Confounds HRV

Background

Decreased HRV is associated with increased mortality

- In cardiac patients
- In population studies

(e.g., Framingham, Cardiovascular Health Study)

Therefore ….

decreased HRV is bad

increased HRV is good.

Evidence to the Contrary

Zutphen Study

HRV from 25-30-s strips from resting 12-lead ECGs

5-year, age-adjusted risk of mortality for low HRV 2.1 in middle-aged and 1.4 in elderly men.

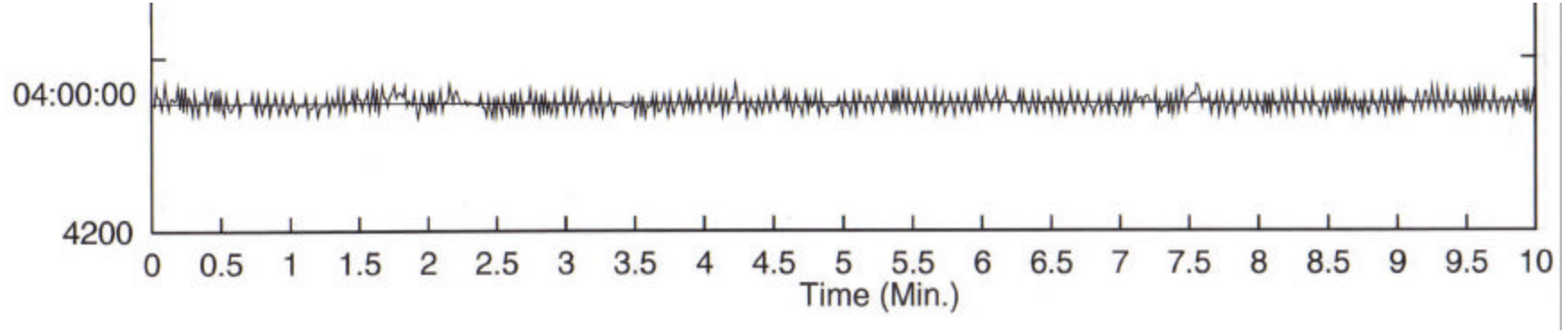
Higher HRV in older men did not appear to reflect RSA, and associated with increased mortality.

Dekker JM, et al. Am J Epidemiol 1997;145:899-908.

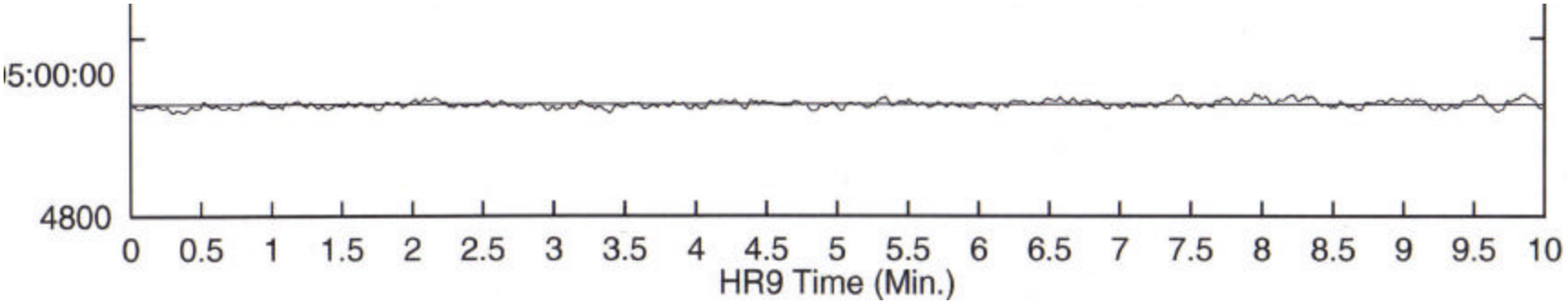
Confounders and Caveats for HRV and Autonomic Function

- HRV may not be meaningful in patients with a high degree of non-respiratory sinus arrhythmia (Erratic Sinus Rhythm).
- Associated with abnormal-looking, blurred power spectral plot
- Often episodic. High prevalence exaggerates HRV
- Abnormal respiration may also produce abnormal plots and exaggerated HRV

Randomness vs. RSA
10-Min Heart Rate Tachograms

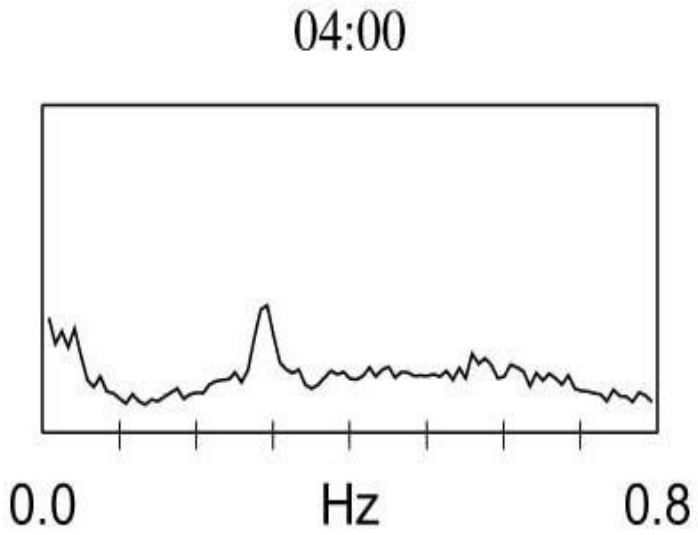


Heart Rate Tachogram for SCD Case

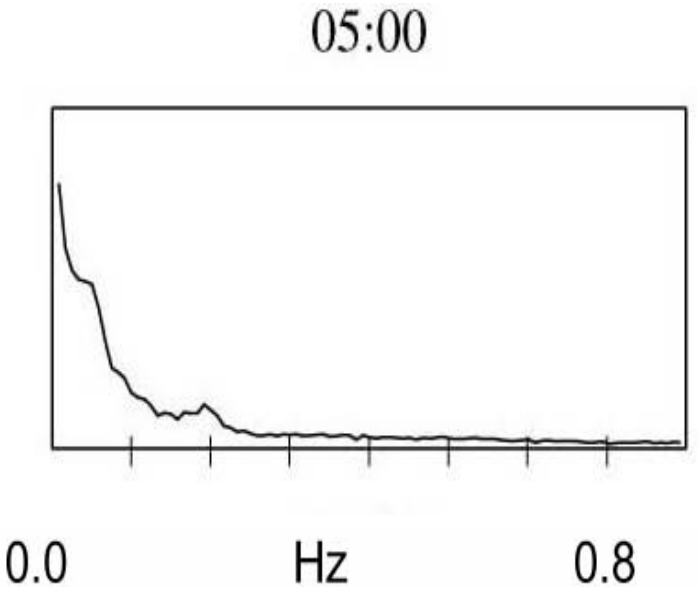


Heart Rate Tachogram for Control

Randomness vs. RSA
One Hour Power Spectral Plots

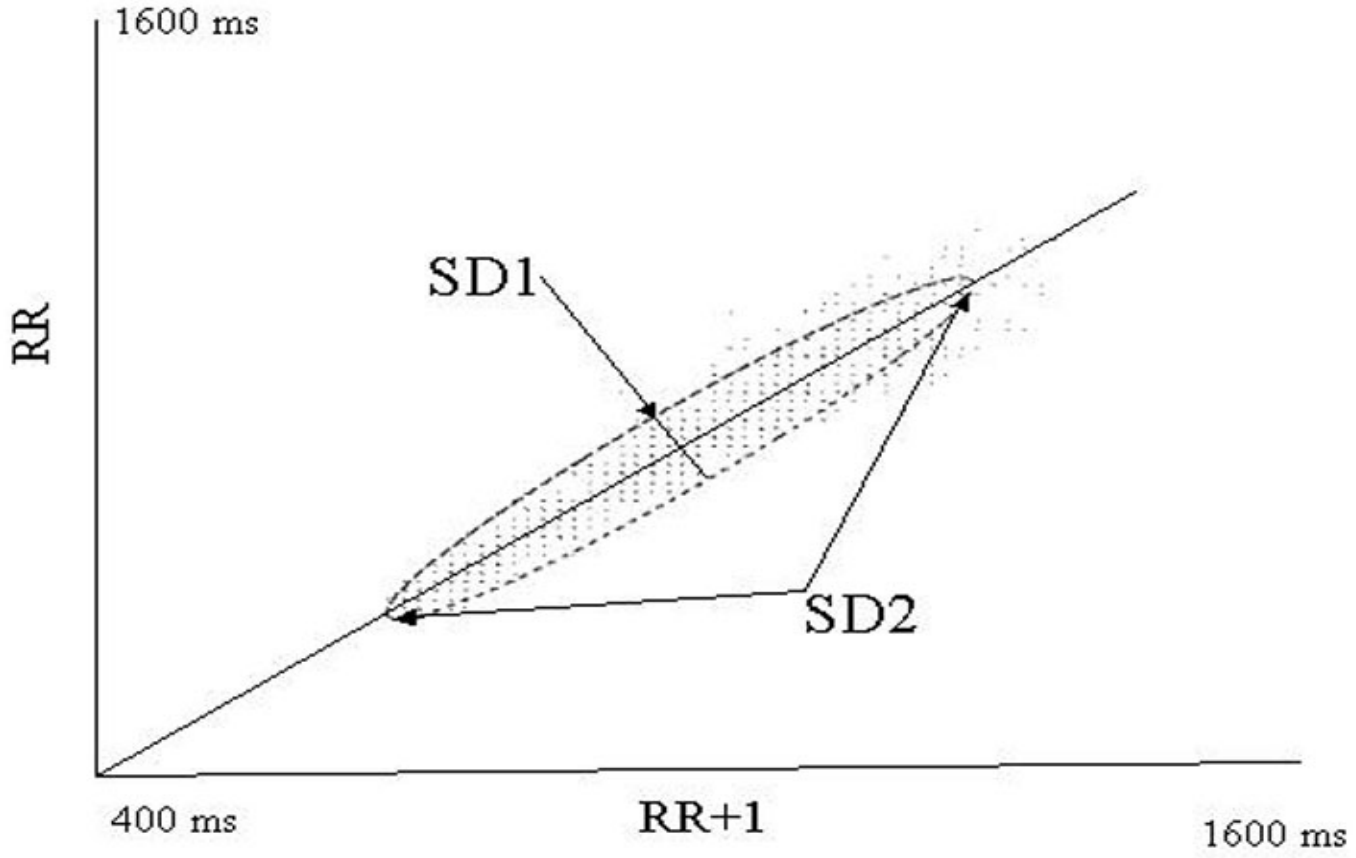


Abnormal FFT for SCD case

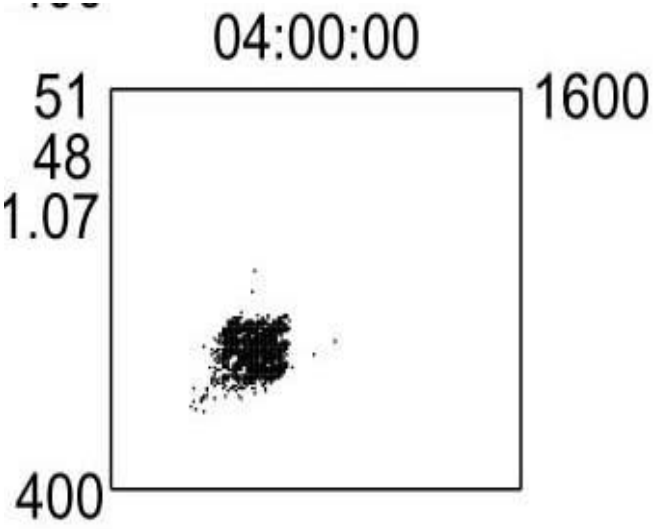


Normal FFT for Control

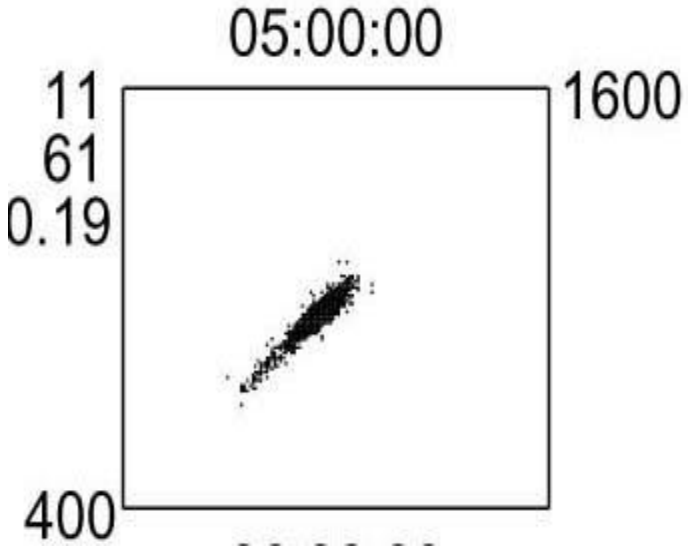
Poincare Plot to Measure SD12 of N-N Intervals



Randomness vs. RSA
Hourly Poincaré Plots



Poincaré plot for SCD case

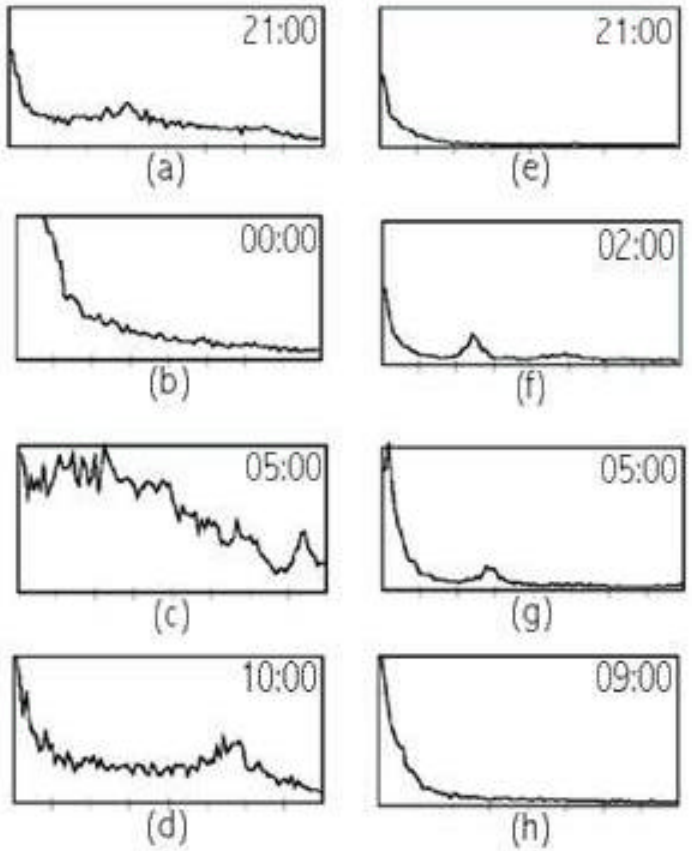


Poincaré plot for control

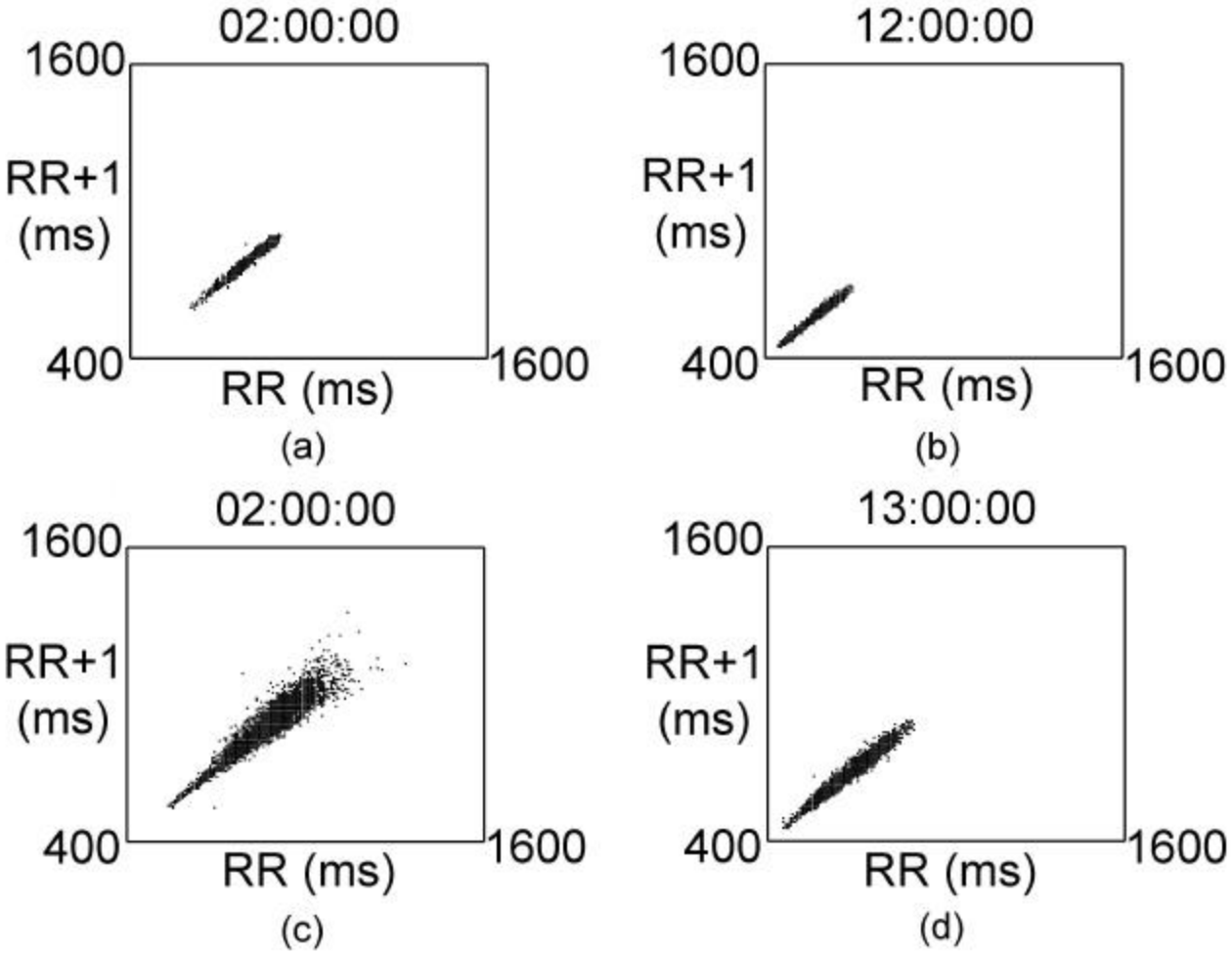
Cardiovascular Health Study (CHS) Holter Cohort

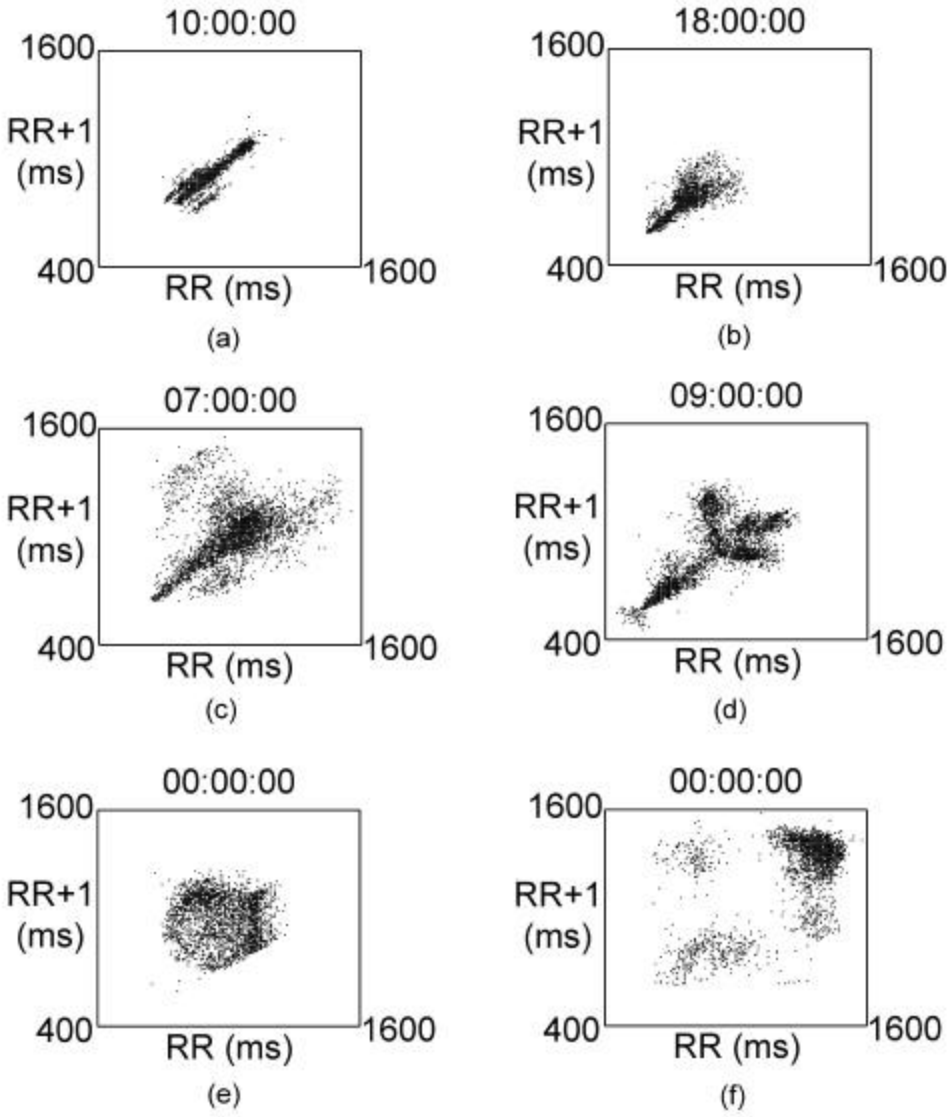
- Age>65 yrs.
- Followed 1988-2002
- N=1429 Holter recordings at yr2 and N=864 at yr7 in same cohort.
- N=385 Holter recordings at yr7 in new African American cohort.

Comparison of Normal and Highly Abnormal 2-min Averaged Hourly FFT Plots (CHS)



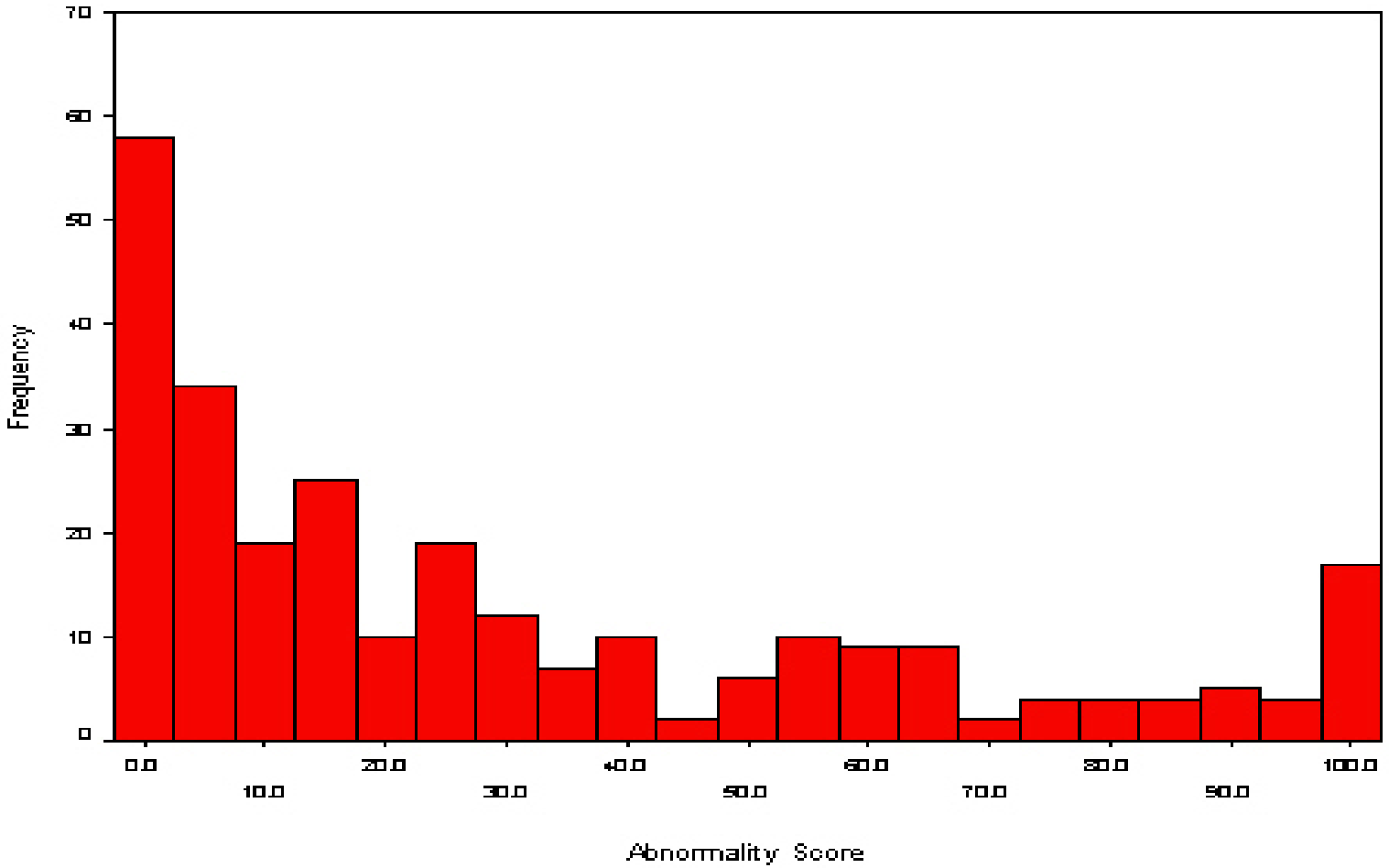
Normal-Appearing Hourly Scatterplots (CHS)





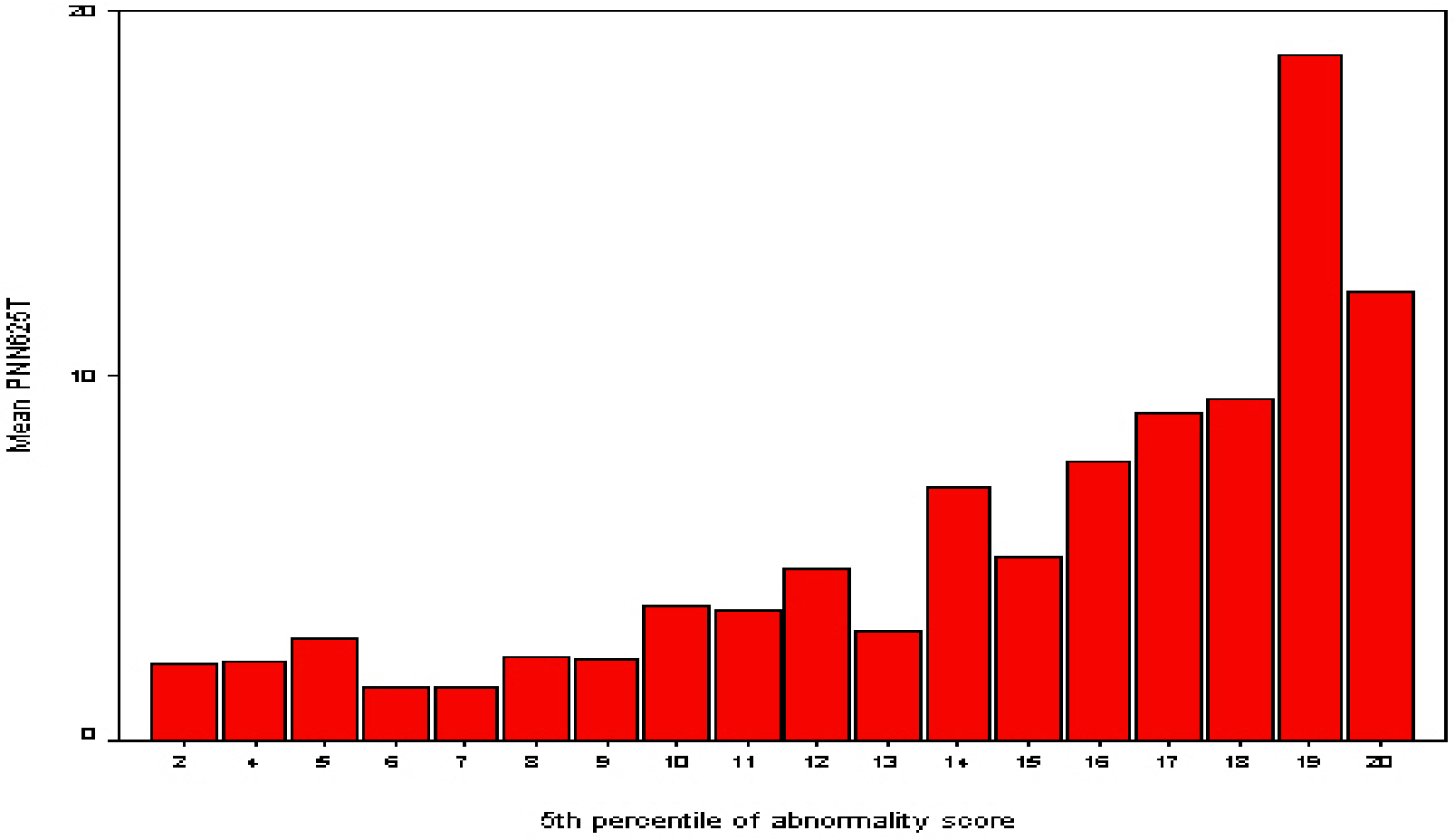
Abnormal (Complex) Hourly Scatterplots From the CHS

Distribution of Abnormality Scores in the CHS



Stein et al., JCE;16:954-9:2005

Effect of Abnormality Score on pNN625 in the CHS



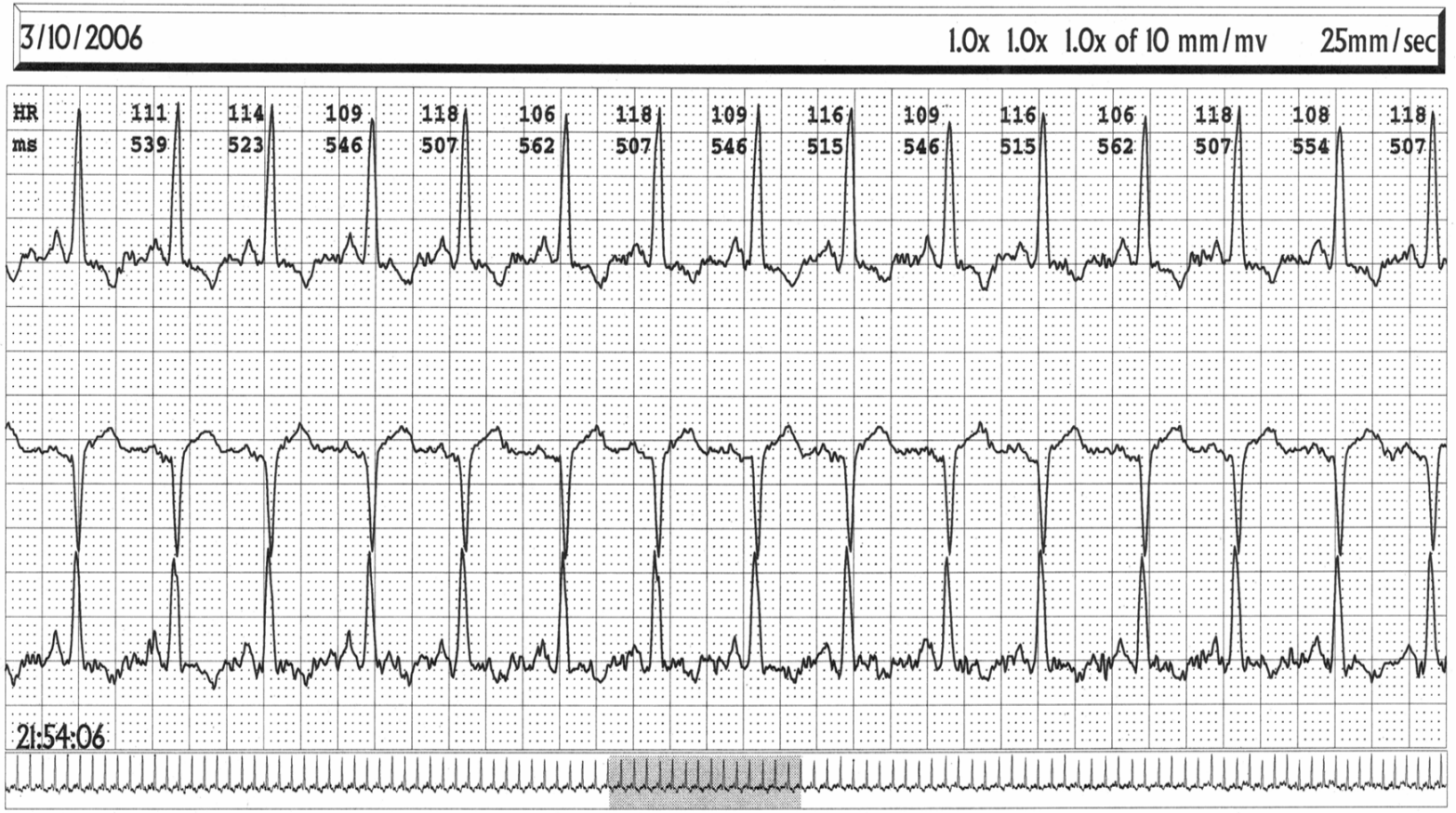
Stein et al., JCE;16:954-9:2005

Comparison of 24-Hour Frequency Domain and Non-Linear HRV for Subjects Above (N=63) and Below (N=198) the Cutpoint for Markedly Increased Short-term HRV in the CHS.

	Above	Below	p-value
Ln TP	9.40 ✂ 0.71	9.57 ✂ 0.04	0.086
Ln ULF	9.24 ✂ 0.71	9.45 ✂ 0.04	0.012
Ln VLF	6.81 ✂ 0.82	6.88 ✂ 0.04	0.501
LF/HF Ratio	2.48 ✂ 1.73	4.70 ✂ 0.15	<0.001
Ln LF	5.92 ✂ 1.00	5.79 ✂ 0.05	0.338
Ln HF	5.52 ✂ 1.21	4.59 ✂ 0.06	<0.001
Norm LF	39.2 ✂ 9.1	48.0 ✂ 0.5	<0.001
Norm HF	28.3 ✂ 9.0	17.0 ✂ 0.4	<0.001
Power Law Slope	-1.291 ✂ 0.126	-1.318 ✂ 0.009	0.154
Alpha1	0.83 ✂ 0.18	1.09 ✂ 0.01	<0.001

Stein et al., JCE;16:954-9:2005

“Sinus” Bigemeny Confounds HRV



HRV and Erratic Rhythm

- Accurate measurement of HRV depends on research quality scanning.
- Erratic rhythm and sinus bigemeny elevate short-term “vagal” HRV.
- Non-linear indices, decreased a_1, increased SD12 reflect erratic rhythm.
- Decreased LF/HF ratio may reflect erratic rhythm.

HRV and Erratic Rhythm

- Longer-term HRV least confounded by erratic rhythm and sinus bigemeny.
- Best predictors may be SDANN and ULF, because beat-to-beat changes in HRV are not included.
- SDANN <100 ms shown to risk stratify in CHF with AF.[1]

1. Frey B et al. Am Heart J. 1995;129:58-65.

HRV in Heart Failure

HRV and Mode of Death in Heart Failure

- HRV may provide different information in ischemic vs. idiopathic etiologies.
- Different risk factors for pump failure vs. sudden death.
- Pump failure more “expected.”
- Sudden death often occurs in patients with better preserved ventricular function.

HRV and All-Cause Mortality in Ischemic Heart Failure

- Generally same results are HRV in post-MI patients.
- Studies often overlap because higher-risk patients recruited for trials.
- In most studies, decreased longer-term HRV adds to predictive value of clinical and demographic risk factors for pump failure only.

Effect of Diabetes on HRV in CHF

	Class II No Diabetes (N=47)	Class II Diabetes (N=40)	Class III No Diabetes (N=32)	Class III Diabetes (N=35)	p-value
Heart rate (bpm)	68 ✂2[a]	72 ✂2	75 ✂2	76 ✂2	0.002
SDNN (ms)	117 ✂6[b]	92 ✂6	91 ✂7	92 ✂7	0.012
SDANN (ms)	102 ✂5[b]	80 ✂5	77 ✂5	79 ✂6	0.003
SDNNIDX (ms)	51 ✂4	39 ✂4	42 ✂5	39 ✂5	0.183
rMSSD (ms)	33 ✂5	31 ✂6	35 ✂6	36 ✂6	0.908
pNN50 (%)	9.3 ✂1.7	7.6 ✂1.8	8.1 ✂1.9	7.8 ✂1.9	0.911

[a] Post hoc analysis, significant differences between class II without diabetes and both class III groups ($p<0.05$).

HRV and Mode of Death in CHF

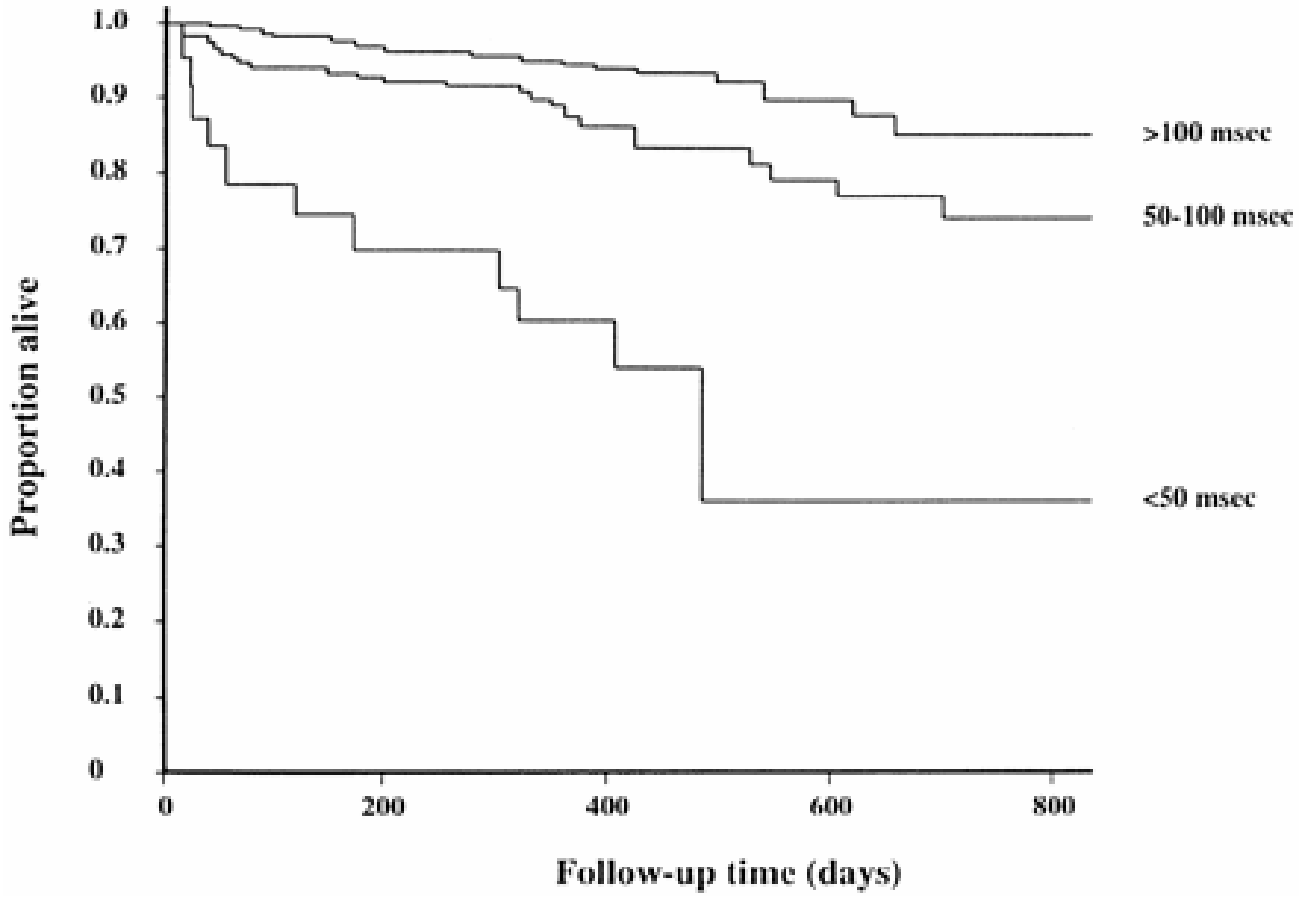
- N=330 consecutive CHF stable for >2wks.
- Etiology roughly ½ ischemic.
- FU = 3 years.
- HRV predictor of pump failure: Night VLF = 509 ms^2 (+PWP = 18 mm Hg, LVEF =24%)
- HRV predictor of SCD: LF= 20 ms^2 (LVESD 61 mm).
- SDNN, power law slope univariate predictors of pump failure/ urgent transplant but not SCD.

Guzzetti S, et al., Eur Heart J. 2005;26:357-62.

Large CHF trials (*Drug Study)

- DIAMOND 1998
- UK-Heart 1993
- Dutch Ibopamine Multicenter Trial* ~1990
- TRACE 1995
- DEFINITE 1998 (ICD study)
- EMIAT* 1990

HRV and Outcome in UK-Heart



Nolan J. Circulation. 1998;98:1510-6.

HRV and Outcome in CHF (DEFINITE)

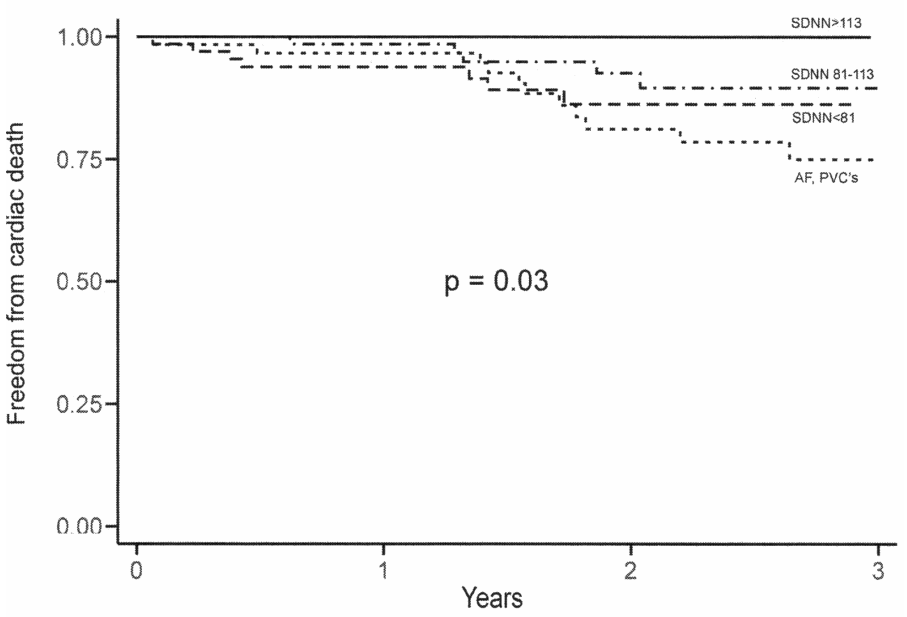


Figure 3 Risk stratification for cardiac mortality, implantable cardioverter-defibrillator (ICD) and medical therapy arms combined. SDNN is categorized in tertiles. Patients who were excluded from heart rate variability analysis because of atrial fibrillation (AF) or frequent ventricular ectopy are analyzed in a separate group. Kaplan-Meier curves of event-free survival are shown, truncated at 3 years.

Rashaba et al, Heart Rhythm 2006;3:281-286.

Sudden Cardiac Death

SCD in the Cardiovascular Health Study (CHS)

- SCD matched 1:2 with no SCD on age, gender, beta blocker use and diabetes.
- Controls alive at the time of death of case no subsequent SCD.
- Recording closest to SCD used if possible. Cases and controls matched on recording used (yr2 or yr7).

Stein et al, Presented at ACC 2005

Subjects CHS SCD Study

	SCD N=52	No SCD N=104
Age (yrs)	73.7 ± 5.2	73.8 ± 5.5
Gender	35M, 17F	70M, 34F
Years to death	6.2 ± 2.4 (0.15-10.4)	7.9 ± 2.9 (2.6-11.6)
% mortality	100	48

Stein et al., Presented at ACC, 2005

Results (CHS)-Time Domain HRV

- No difference in heart rate or time domain HRV, except for significant *increase* in rMSSD and pNN50 among SCD cases.

	No SCD N=104	SCD N=52	p-value
HR (bpm)	73±11	73±10	NS
SDNN (ms)	122±39	118±38	NS
pNN50 (%)	6±8	10±13	0.04
rMSSD (ms)	27±16	35±28	0.05

Stein et al, Presented at ACC 2005

Results (CHS)- Frequency Domain HRV

No difference in traditional frequency domain HRV (TP, ULF, VLF, LF, HF). Significant differences in ratio indices.

	No SCD N=99	SCD N=43	p-value
Ln VLF	6.9±0.7	6.8±0.8	NS
Norm LF	62±12	56±12	0.02
Norm HF	24±10	28±10	0.04
LF/HF	4.3±2.6	3.4±2.2	0.04

Stein et al., Presented at ACC 2005

Results (CHS)-Non-Linear HRV

Short-term fractal scaling exponent [DFA1,(a1)] significantly decreased, SD12 significantly increased among SCD cases.

	No SCD N=99	SCD N=43	p-value
DFA1	1.19±0.22	1.06±0.22	0.002
SD12	0.26±0.11	0.31±0.16	0.03
Slope	-1.36±0.15	-1.37±0.37	NS

Stein et al., Presented at ACC 2005

Results (CHS)- Heart Rate Turbulence and SCD

- HRT(+), defined as turbulence onset >0 or turbulence slope <2.5.
- HRT(+) more prevalent among SCD.
- 49% of SCD had HRT(+).
- 28% no SCD had HRT(+).

(Unpublished data)

Traditional HRV and Risk of Sudden Cardiac Death

- Since half of cardiac deaths are sudden, assumed that HRV is predictor of SCD.
- Identifying SCD problematic but less so in the ICD era.
- Results contradictory, especially for longer-term HRV.

Non-Linear HRV and Risk of Sudden Cardiac Death

- Results in CHS, Turku, Dutch Ibopamine Multicenter Trial, suggest that abnormal non-linear HRV predicts SCD.
- Identification of abnormal non-linear HRV requires research quality scanning.

Heart Rate Turbulence and Risk of Sudden Cardiac Death

- Abnormal HRT (especially TS) strong predictor of cardiovascular death.
- No clear evidence of strong relationship between HRT and SCD.

Summary

- Erratic rhythm is associated with abnormal non-linear HRV, but elevates some traditional HRV measures.
- Decreased SDNN predicts mortality in CHF.
- Abnormal non-linear HRV may predict sudden death.

Final Thoughts

- Many large Holter datasets available to test HRV and outcome.
- Many fewer datasets with research quality scanning.
- Further studies with more careful data analysis needed to derive usable measures of HRV to risk stratification.