



HRV and Risk Stratification: Post-MI

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Outline

- Research vs. clinical Holter scanning.
- Caveats in interpretation of published studies.
- HRV predictors of mortality post-MI.
- What is the “best” HRV for risk stratification?
- HRV in combination with other risk factors.

Clinical vs. Research Holter Analysis

- Research-quality Holter scanning ?
Clinical scanning.
- Clinical Holter scanning focuses on efficiently finding arrhythmias and ST changes.
- Precise HRV analysis is time-consuming and requires careful attention to beat-labeling and beat onset detection

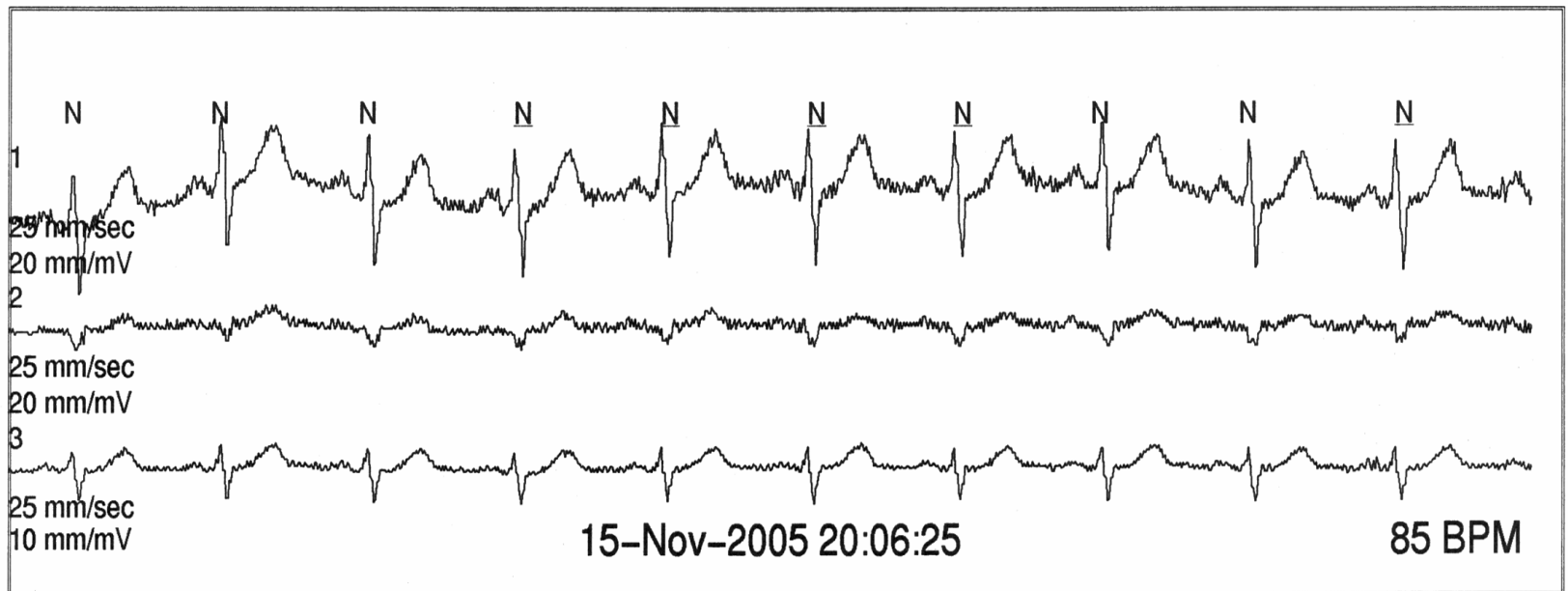
Clinical vs. Research Scanning

- Technician accuracy -how far the technician is willing to go to characterize the recording.
- May be a function of time pressure in clinical lab.
- Limitations of the Holter scanning system, including flagging of premature beats and accurate beat detection.

Beat Detection Issues

- Many Holter analysis systems have no way to verify uniformity of beat detection.
- Not enough to have accurate beat labels.
- Non-uniform beat detection can exaggerate HRV and distort frequency domain and non-linear HRV.

Uneven Beat Detection



Uniform and accurate beat-to-beat interval measurement is essential for many, but not all, ambulatory ECG-based risk predictors!

Comparison of Results from Different Scanning Systems

- N=26 post-MI patients
- HRV calculated 4 times each by a different technician using 3 different scanners (one twice).
- AVNN, SDNN, rMSSD and triangular index (TI) calculated.
- AVNN most similar. SDNN and TI not significantly different. rMSSD was significantly different.

Does It Have to be A 24-Hour Recording?

- Patient with very low HRV will have very low HRV on a short recording.
- Bigger et al¹ showed that HRV from randomly-selected short (2-15 min) segments correlated with 24-hour HRV (mostly = 0.75) and were excellent predictors outcome in MPIP.
- St. George's group² showed that 5-min recordings could identify subset that needed longer recording for risk stratification so that prediction from subset similar to prediction from entire cohort.

¹Bigger JT et al. Circulation. 1993;88:927-34 ²Fei L et al. Am J Cardiol. 1996;77:681-4.

Some Large Post-MI Trials

(*Also Drug Trials)

- MPIP 1983 AMI
- GREPI 1988 Post-MI
- *CAPS 1989 1 yr post-MI
- ATRAMI 1998 AMI
- GISSI-2 1990 AMI
w/thrombolysis
- *EMIAT 1990 AMI + CHF
- *CAST 1992 Various times post-MI
- St. George's group AMI

When Was HRV Measured?

- Within 2-3 days post-MI? (TRACE)
- Pre-discharge. (Most St. George's)
- Two weeks post-MI (not specified if inpatient or outpatient).
- At a range of times post-MI (CAST).
- One-year post-MI (CAPS).

Recovery of HRV Post-MI

- HRV lower in post-MI than in healthy controls.
- HRV increases with recovery.
- Unclear how long HRV continues to improve, suggested to be 3-6 months.
- Cutpoints for risk post-MI may be function of recovery point and higher risk in early post-MI period.

Effect of CABG and Diabetes on HRV Risk Stratification

- HRV and HRT markedly depressed post-CABG, probably 6 mos-1 yr to recover. (TS no recovery).¹
- Decreased HRV post-CABG not associated with mortality.²
- CAST Study-Inclusion of diabetics or post-CABG markedly reduced association of HRV and mortality.³
- MPIP-Diabetics much higher mortality, but similar cutpoints (only InTP reported) risk stratified both groups.⁴

1. Cygankiewicz I et al. Am J Cardiol. 2004;94:186-9. 2. Milicevic G et al. Eur J Cardiovasc Prev Rehabil. 2004;11:228-32 3. Stein PK et al. Am Heart J. 2004;147:309-16 4. Whang and Bigger Am J Cardiol 2003;92:247-251.

Perspectives in Traditional HRV

- Longer-term HRV-quantifies changes in HR over periods of >5 min. Includes HRV index.
- Intermediate-term HRV-quantifies changes in HR over periods of <5 min.
- Short-term HRV-quantifies changes in HR from one beat to the next
- Ratio HRV-quantifies relationship between two HRV indices.

Results of Large Post-MI Trials (Traditional HRV Measures)

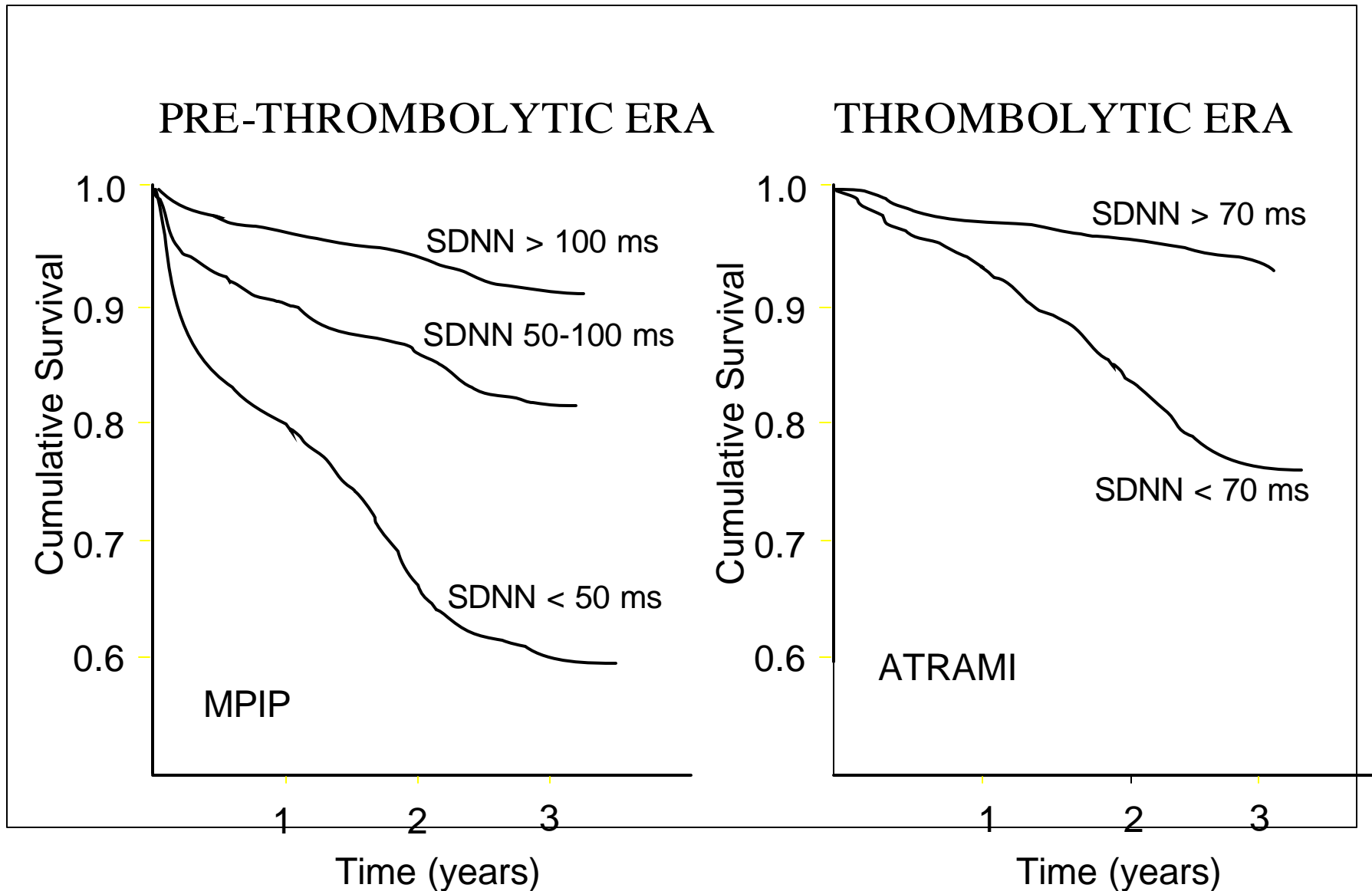
- In general, decreased longer-term HRV, is associated with increased mortality.
- Longer-term HRV measured in different ways including: SDNN, SDANN,TP, ULF, TI.
- In some studies decreased In VLF associated with increased mortality.
- In most studies, short-term HRV not associated with outcome.

Time Domain HRV for Risk Stratification Post-MI

MPIP-SDNN<50 ms after adjustment, relative risk of mortality post-MI = 2.7 compared with SDNN>100 ms, PPA=33%

ATRAMI-SDNN<70 ms, after adjustment, relative risk of mortality post-MI=3.2, PPA=10.6%

SDNN and Mortality Post-MI



Frequency Domain HRV and Outcome Post-MI

MPIP (Mortality)
Multivariate:
Decreased ULF
power (RR=2.3) +
VLF power (2.1)
Combined
PPA=48%

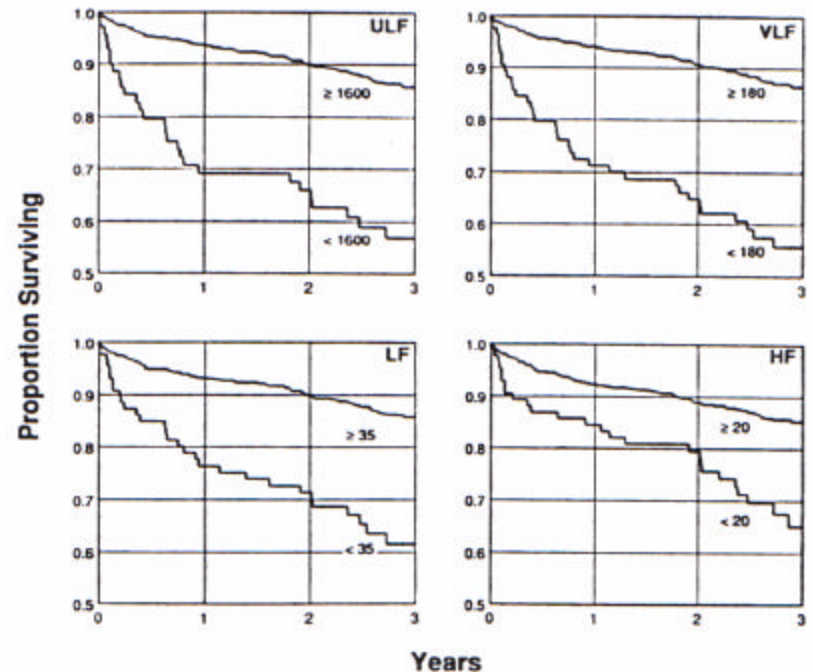


FIGURE 1. Kaplan-Meier survival curves for 715 patients in the high or low category for the four mutually exclusive frequency domain measures of heart period variability—ultra low frequency (ULF), very low frequency (VLF), low frequency (LF), and high frequency (HF) powers—using all-cause mortality as the end point.

Non-Linear HRV and Mortality

- MPIP¹ reanalysis-decreased power law slope most powerful predictor of mortality (not replicated).
- TRACE² (patients AMI and wall motion abnormalities)-decreased short-term fractal scaling exponent independent predictor of mortality.

Results from TRACE

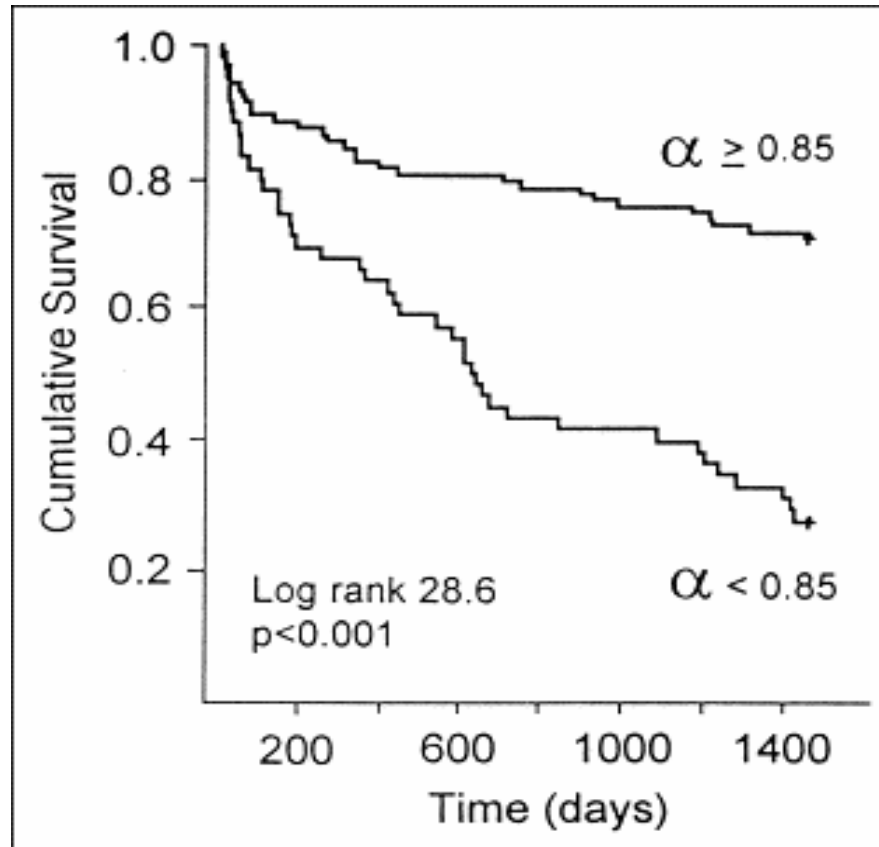
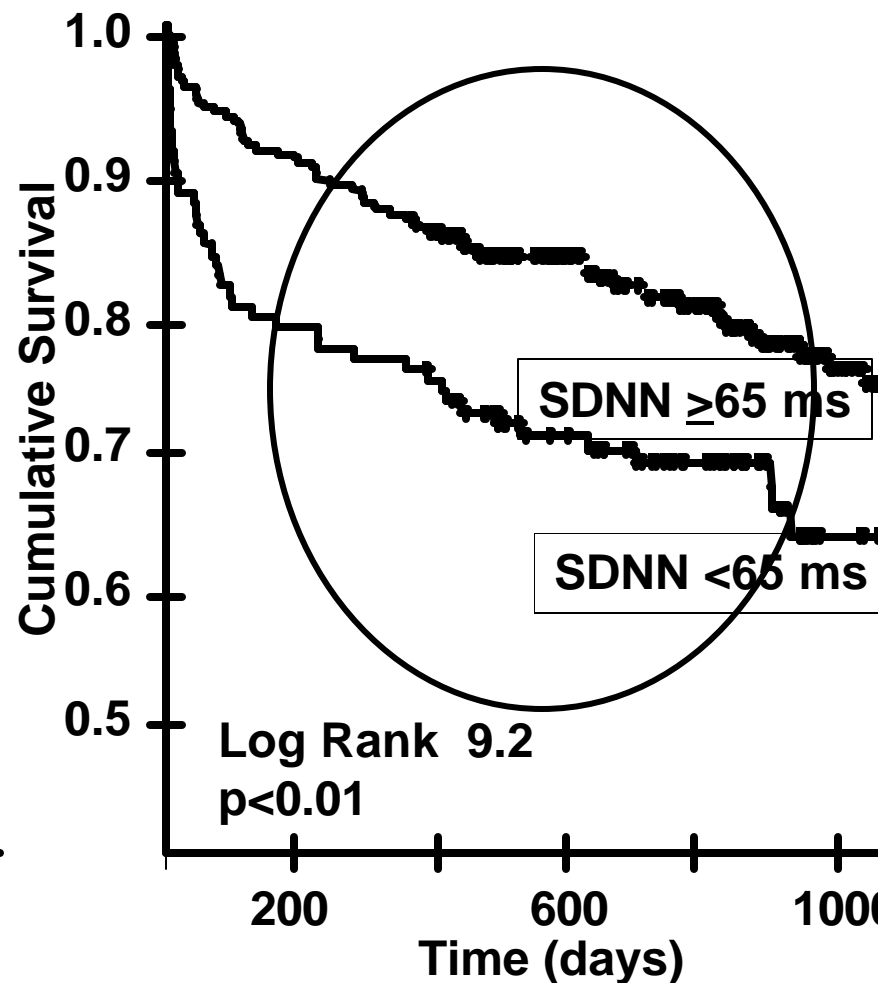
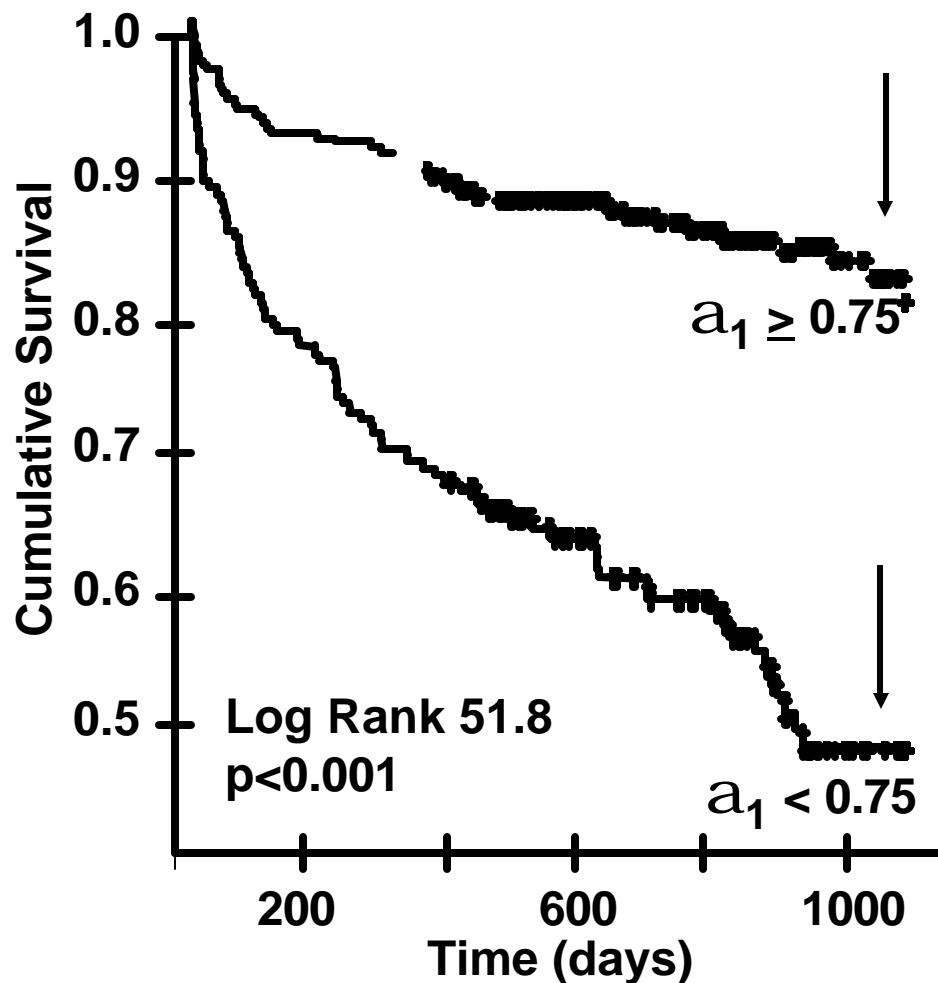


Figure 1. Kaplan-Meier survival curves for the subjects with short-term fractal-like scaling exponent (α) < 0.85 or ≥ 0.85 . Estimated cumulative survival rate over a 4-year period was 70% with an exponent ≥ 0.85 and 28% with an exponent < 0.85 . Mäkikallio et al., Am J Cardiol. 1999;83:836.

Comparison of SDNN and a_1

DIAMOND-CHF



Prediction of Mortality from HRT

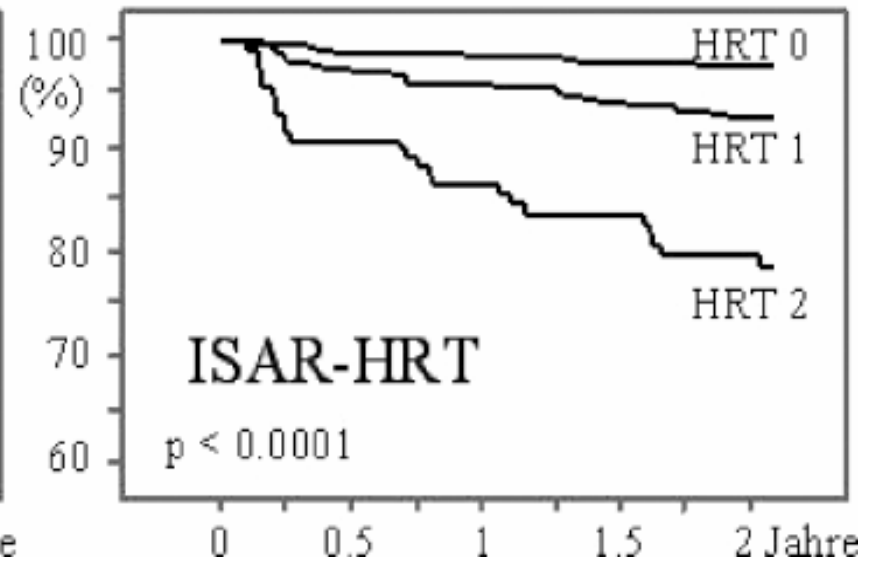
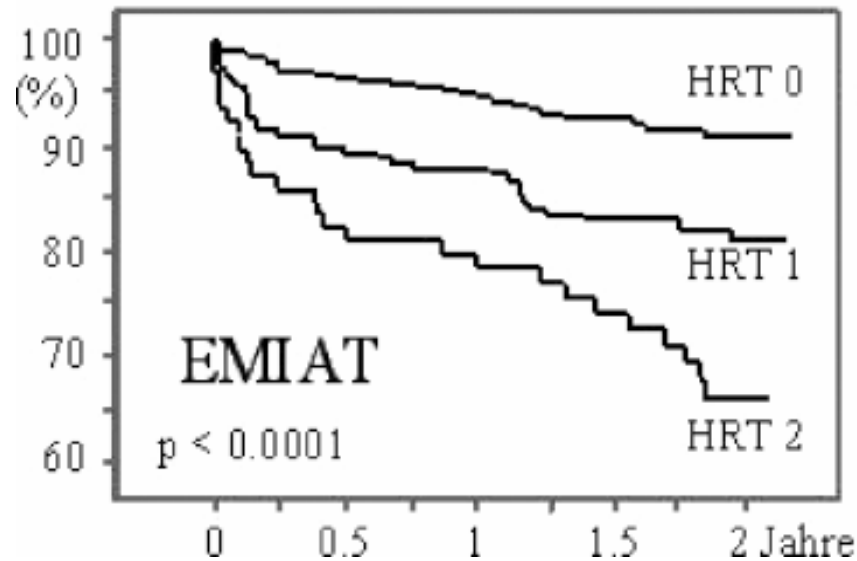
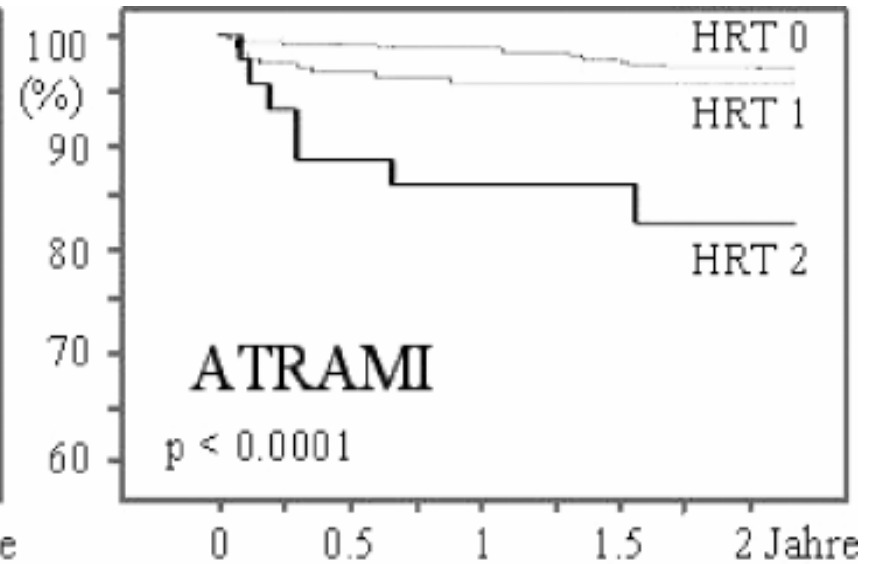
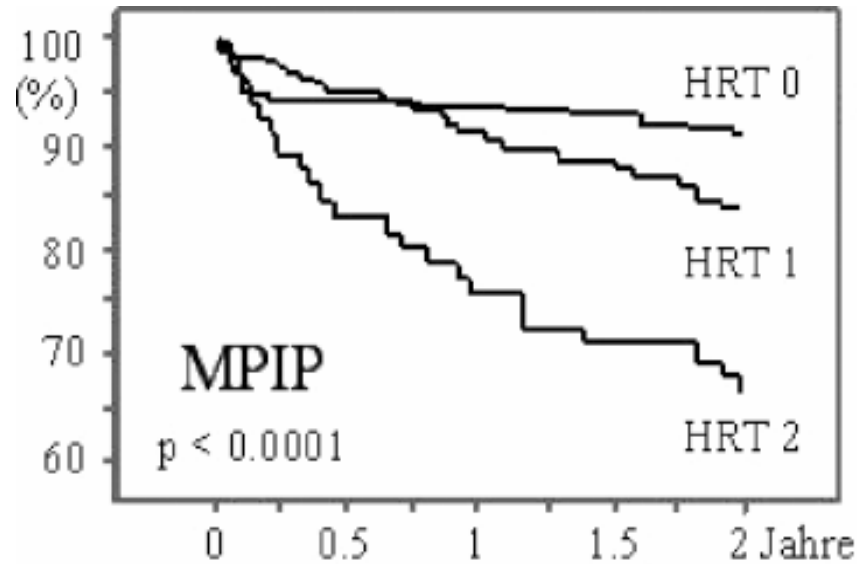
TS<2.5 ms/beat, TO>0 cutpoints for higher risk (dichotomous variable).

MPIP-(Mortality)-TS second strongest risk stratifier (RR=3.5, PPA 27%) after LVEF <30%.

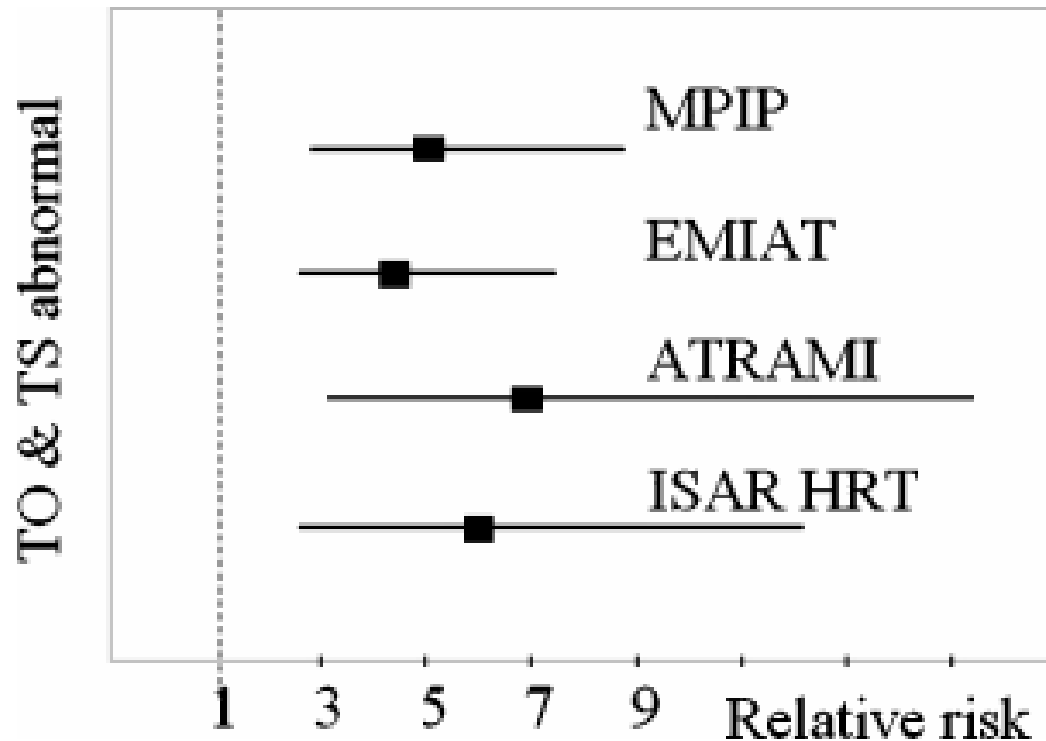
ATRAMI-(Cardiac arrest)-univariate, TS (RR=4.1, PPA=11.6%), TS+TO (RR=6.9, PP=17.6%).

Limitation: Not all patients have enough VPCs (can classify as low risk) or enough time with NSR between VPCs to calculate HRT

Survival Curves Using HRT for Risk Stratification



Comparison of Predictive Value of Abnormal HRT from Different Trials



Adapted from Johnson F et al. A.N.E. 2005;10:102-109.

What is the “best” HRV for risk stratification?

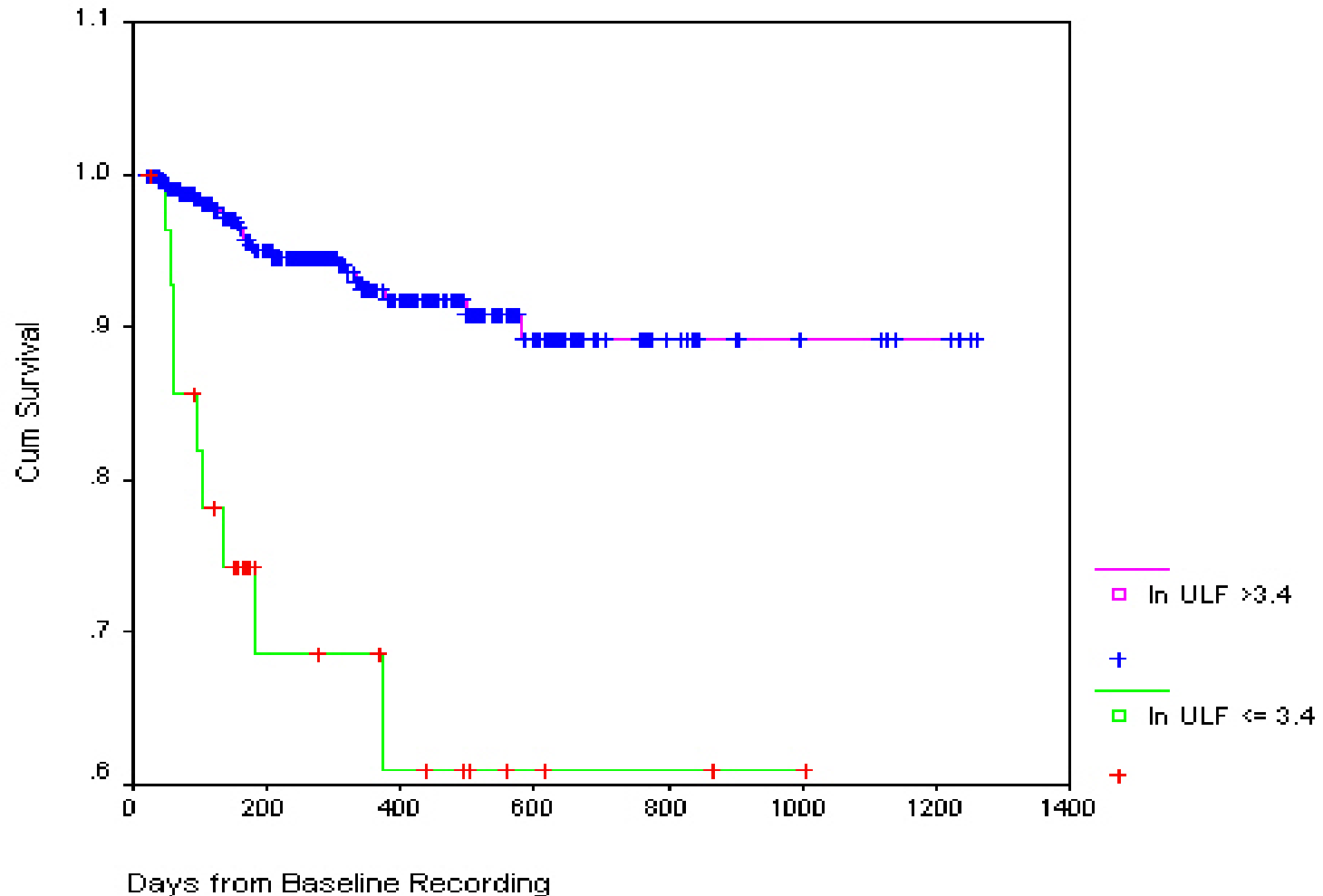
Combinations of HRV Indices May Improve Risk Stratification

- Longer-term HRV, non-linear HRV and HRT measure different aspects of cardiac autonomic functioning.
- Correlations between these indices are weak.
- Possibly combining these indices will improve risk stratification.

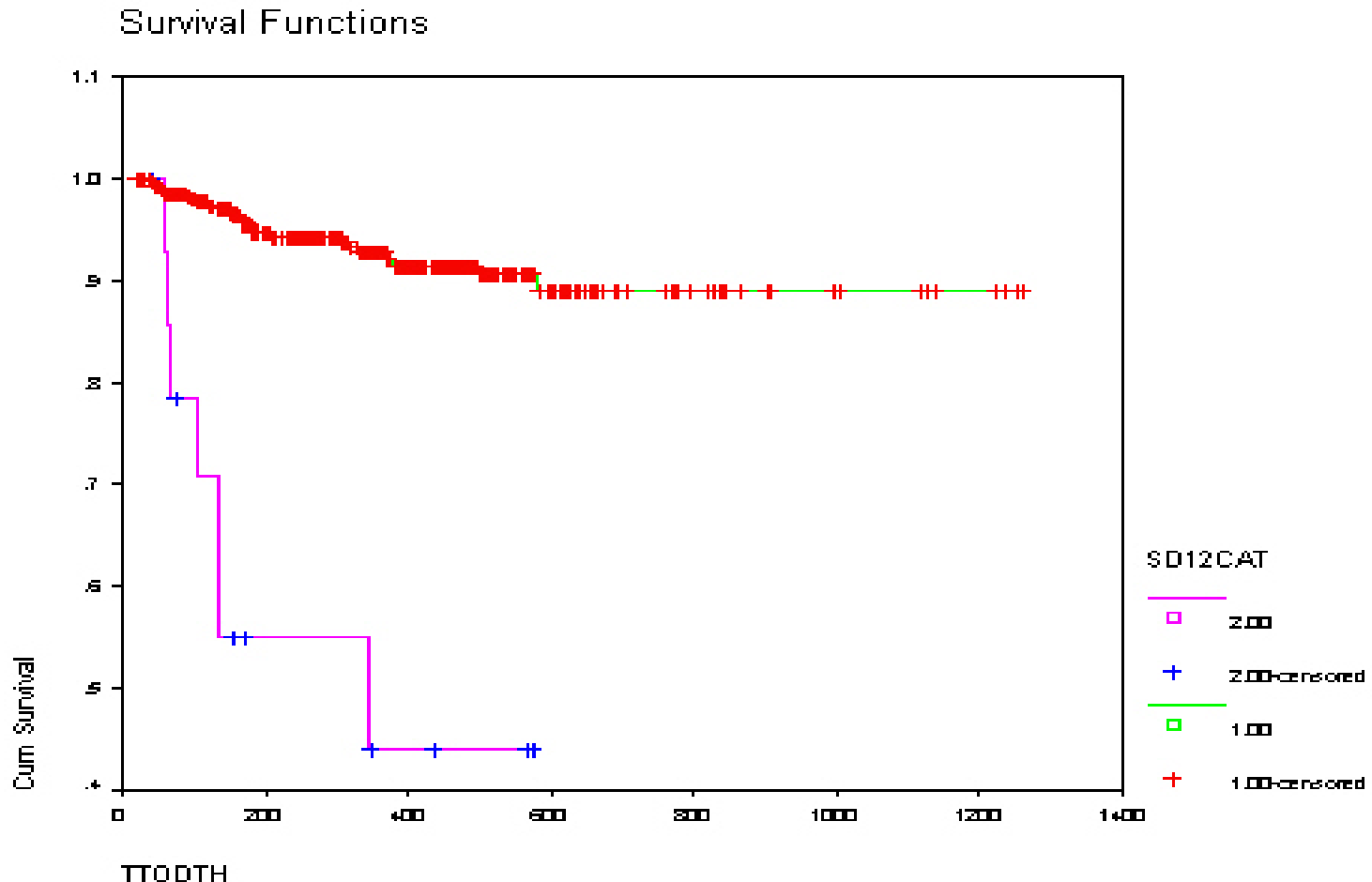
Combinations of HRV Indices for Risk Stratification

1. ATRAMI- SDNN <70 ms + abnormal TO or TS significantly associated with mortality.
2. CAST- Decreased In ULF + increased SD12 independent predictors of mortality in patients without CABG or diabetes. (TS strong predictor in separate analysis).

Survival for Ln ULF Above and Below Cutpoint (3.4) in CAST



Survival for SD12 Above and Below the Cutpoint (0.55) in CAST



Independent Predictors of All-Cause Mortality in the CAST (N=391,32 deaths, no CABG, no diabetes)

	Wald Chi-Sq	p-value
Ln ULF	9.67	0.002
SD12	6.94	0.008
Hx of MI	9.38	0.002
Hx of CHF	5.27	0.022

Combinations of HRV Indices for Risk Stratification

Cardiovascular Health Study (12.3 yr FU)

1. Decreased SDANN + increased rMSSD + abnormal HRT strong independent predictor of CV mortality (Time domain).
2. Decreased ln TP + increased SD12 + abnormal HRT independent predictor of CV mortality in median (Frequency domain and non-linear).

Confounders of HRV for Risk Stratification

- Age
- Gender
- Race (?)
- Metabolic syndrome or diabetes
- Medications
- Physical fitness
- Smoking
- Depression

HRV in Combination with Other Risk Factors

- No one clear set of adjunct risk factors.
- Useful risk factors include: high heart rate, decreased LVEF, frequent VPCs, abnormal signal-averaged ECG.
- Potentially useful: abnormal TWA.

HRV in Combination with Other Risk Factors (MPIP)

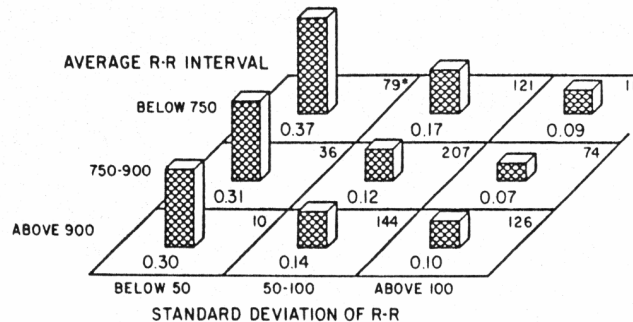


FIGURE 2. Heart rate variability and average heart rate vs mortality.

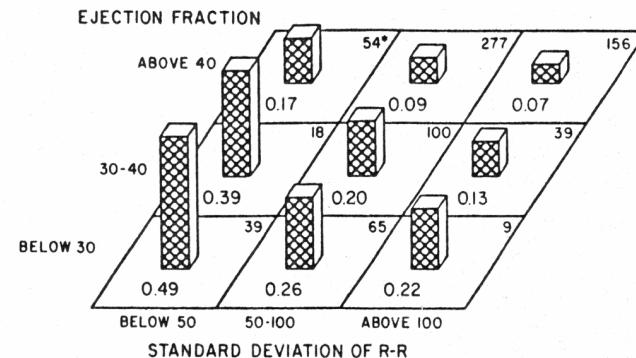


FIGURE 3. Heart rate variability and ejection fraction vs mortality.

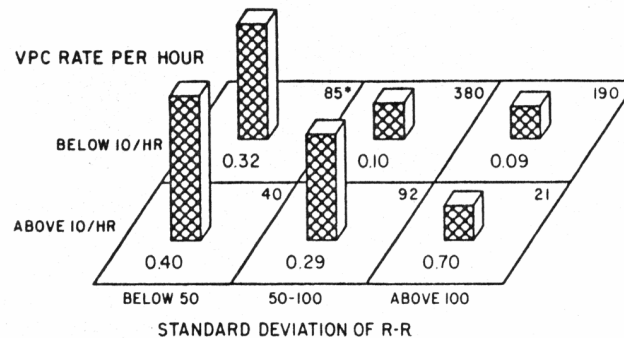


FIGURE 4. Heart rate variability and ventricular premature complex (VPC) frequency vs mortality.

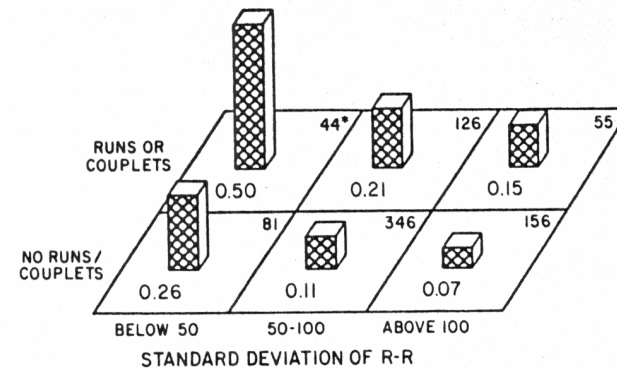


FIGURE 5. Heart rate variability and repetitive ventricular depolarizations vs mortality.

Final Thoughts

- Focus has been on identifying high risk post-MI patients.
- Normal HRV without other major risk factors identifies population at low risk of adverse events, both among cardiac patients and in the general population.

Summary

- Clinical scanning is not usually adequate for detailed HRV analysis.
- Results of studies of HRV and outcome must be interpreted with caution because of different patient populations and recording circumstances.
- Combined HRV indices (longer-term+non-linear+HRT) may provide better risk stratification.
- HRV in combination with other risk factors helps identify high risk post-MI patients.