ROLE OF THE SIGNAL ECG IN RISK STRATIFICATION OF SCD.

An overview

Nabil El-Sherif, MD
SUNY - Downstate Medical Center &
New York harbor VA Healthcare System
Brooklyn, NY, USA

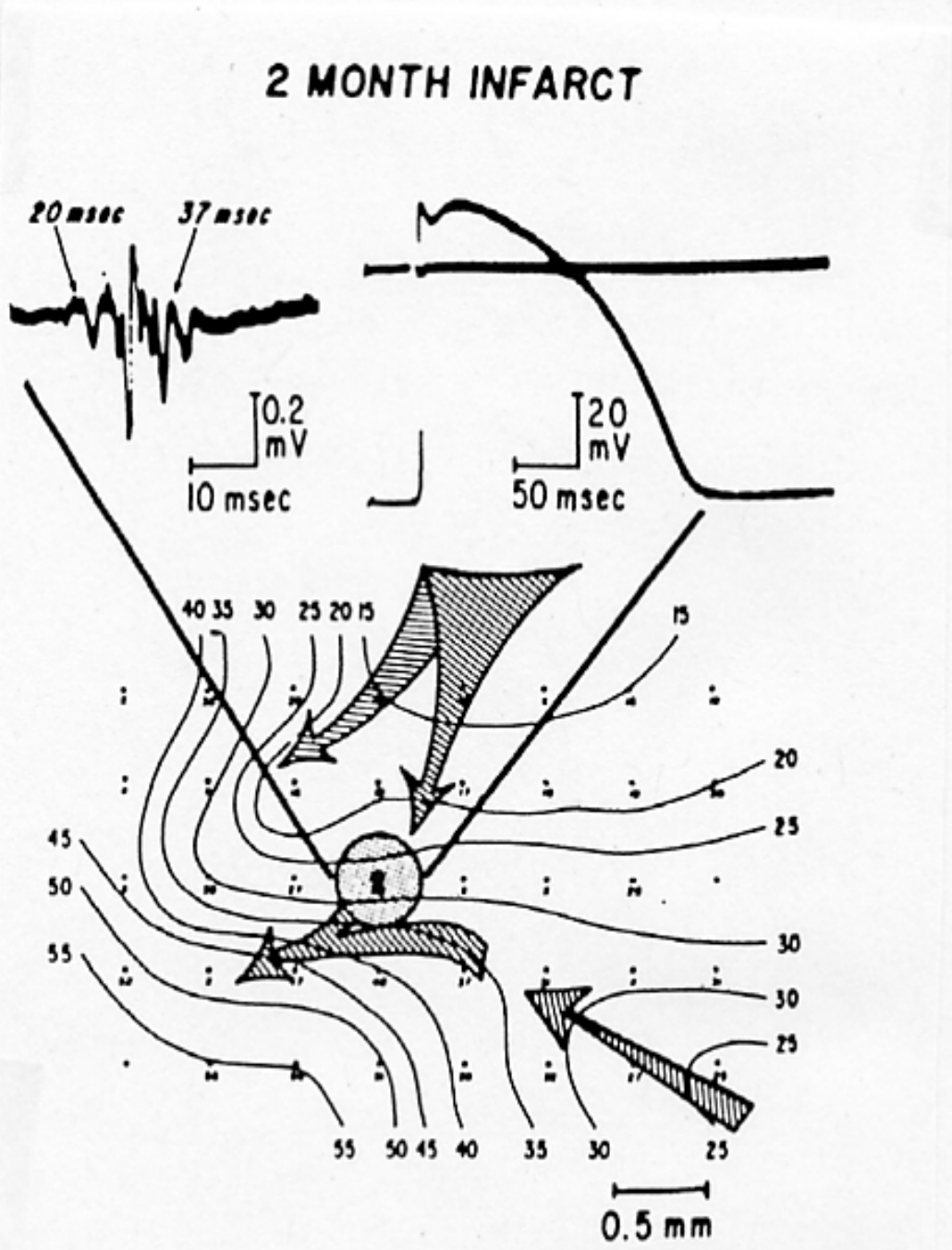
Signal Averaged ECG: A Selective History

- **A) Initial interest focused on recording the His bundle electrogram from the body surface (Ed Berbari: Master thesis, U. Miami, Fl 1973)**
- **B) Interest later shifted to recording of so called "late potentials". This interest was based to, a large extent, on experimental studies in the 1970s by El-Sherif and associates in the canine post-MI heart showing so called "fractionated electrograms" that span the diastolic interval during reentrant VT**

Activation maps of Regions around Bipolar electrodes in Canine 2 months infarct.

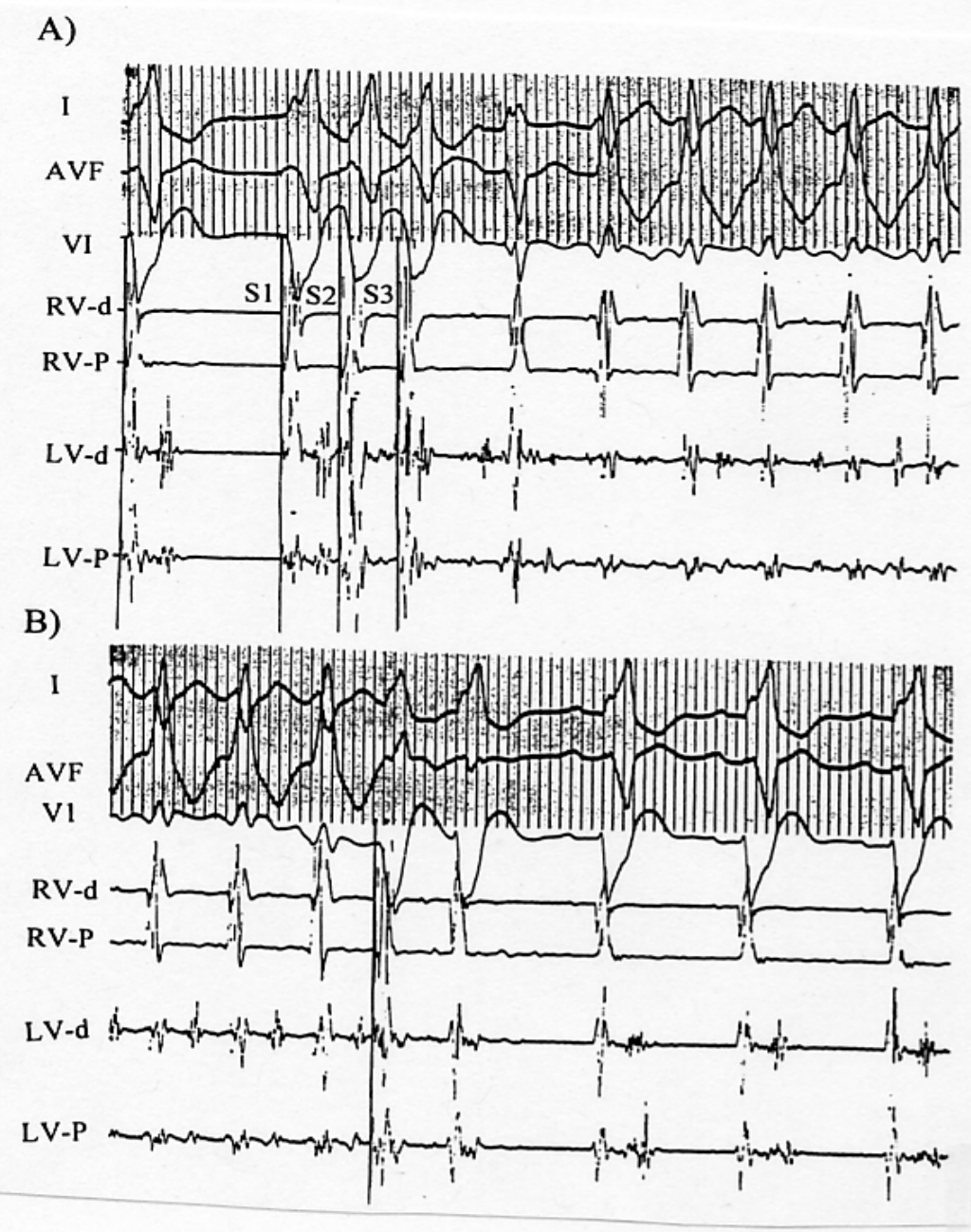
The fractionated Electrograms correspond To to slow and Inhomogeneous Conduction in scarred Infarct with viable Myocardial bundles.

Gardner et al,Circulation 1985;72:596-611



Recordings of bipolar electrograms from the RV and LV from a Patient with inducible Monomorphic VT showing late potentials from LV sites during Sinus rhythm and Fractionated diastolic Potentials spanning the diastolic interval During VT. In B) a Premature stimulus that Terminated VT was not Followed by late potentials

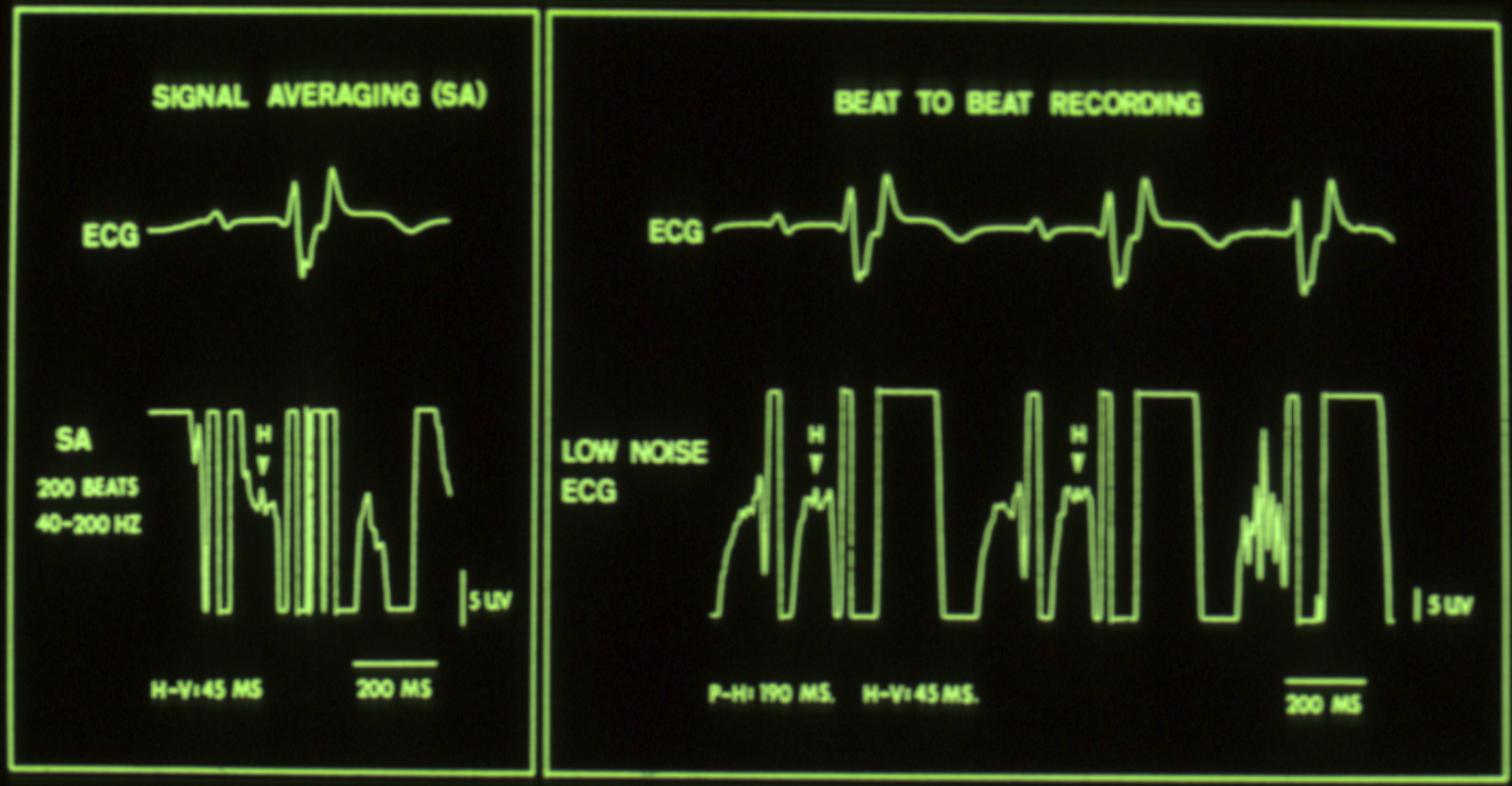
(El-Sherif, In:Interventional Electrophysiology, 1996, Saksena& Luderitz, eds).



The signal averaged ECG
Recording Techniques

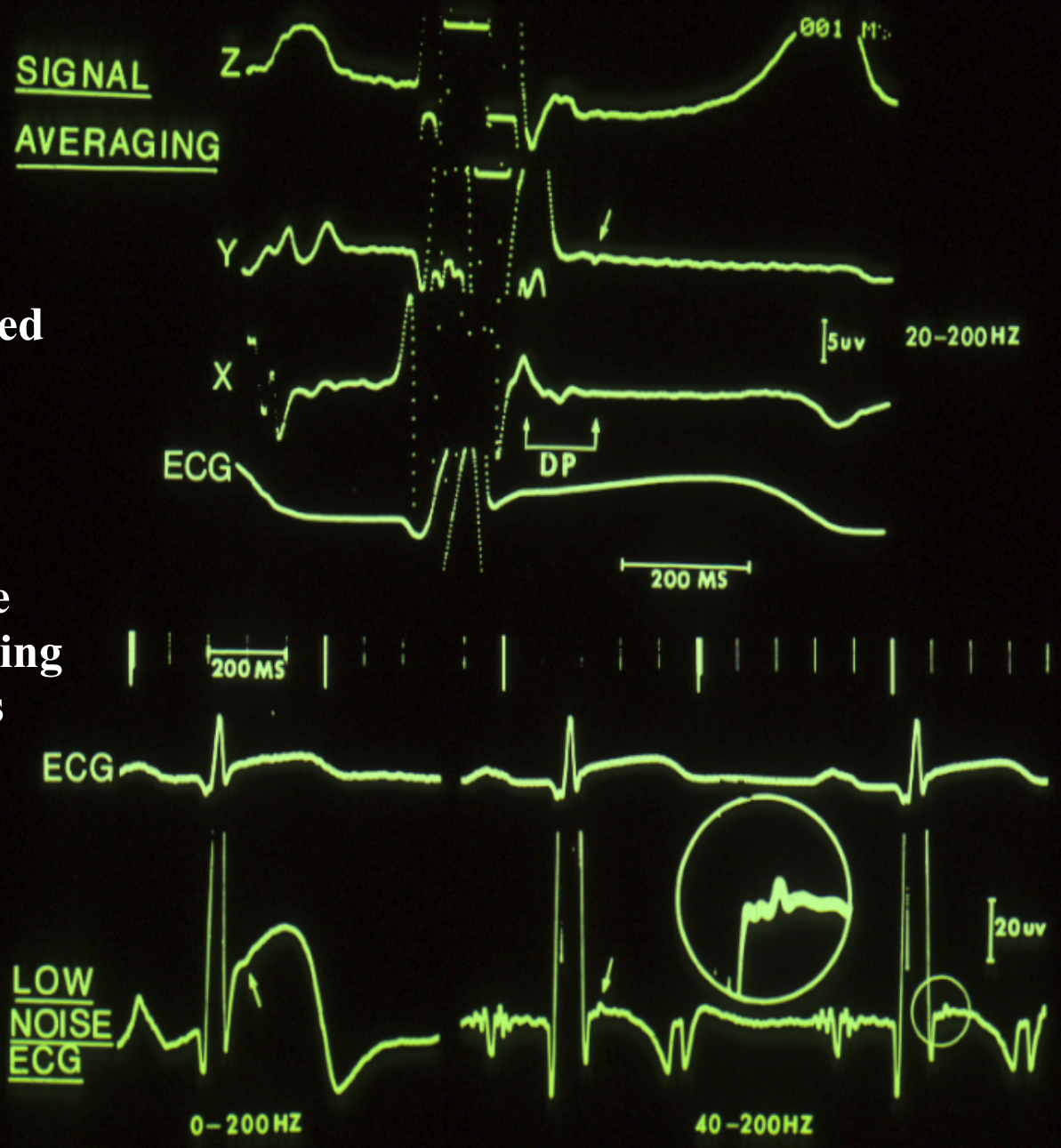
- Ensemble or temporal averaging
  (signal averaging)
  - time-domain analysis
  - frequency-domain analysis

- Spatial averaging



Comparison of Signal Averaging and Spatial Averaging , the latter shows a beat-to-beat recording. Both recordings show the His bundle electrogram

Signal averaged ECG And Spatially averaged ECG from the same Patients showing late potentials



Limitation of Time-domain Analysis of SAECG

- Sensitive to filter setting
- Sensitive to site of MI: ↑ false +ve in IWMI; ↑ false –ve in AWMI

Selected chronological list of different techniques for Frequency-domain Analysis of SAECG

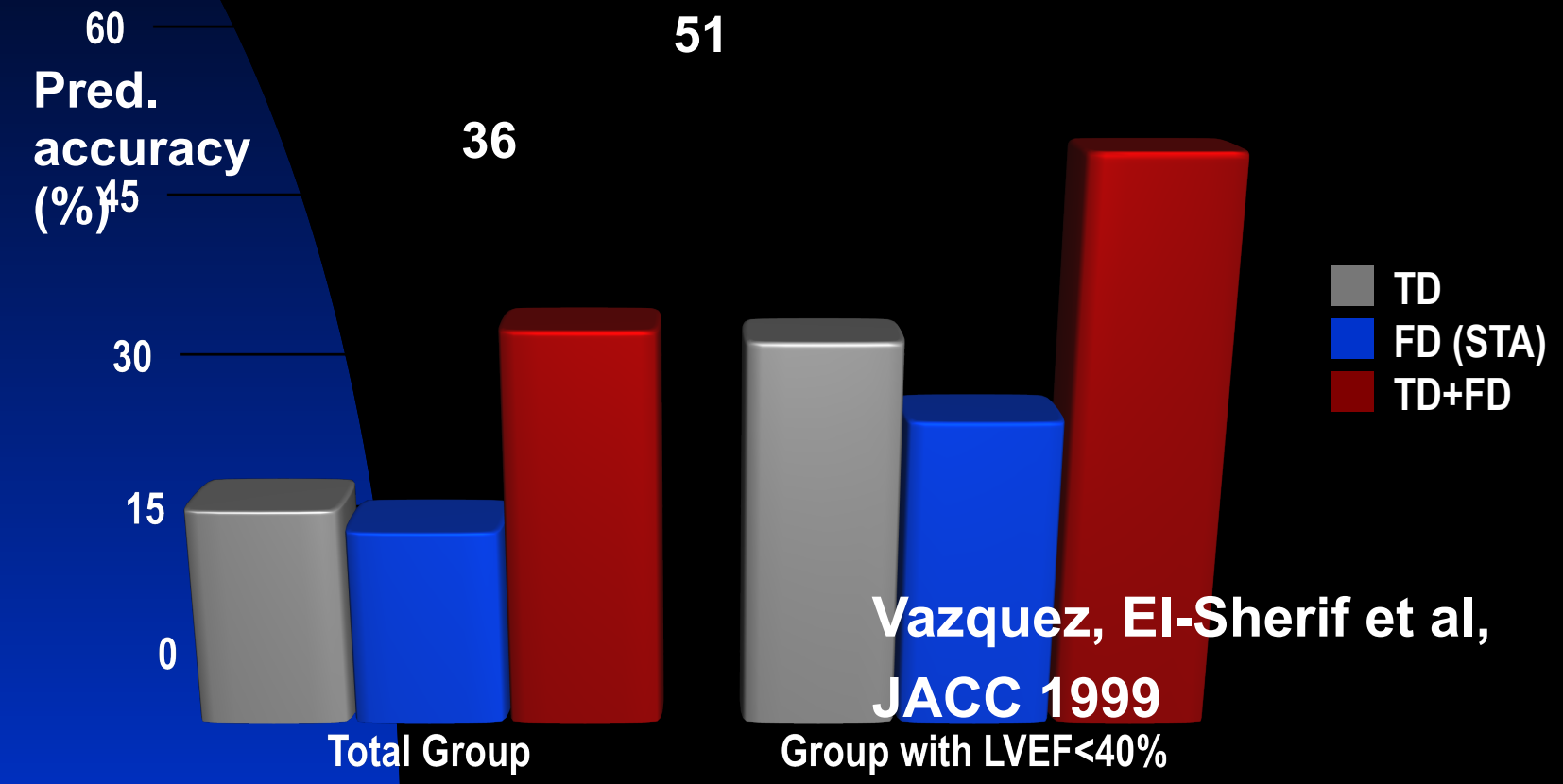
- Cain et al — Spectral Analysis (area ratio)
- Berbari et al — Spectrotemporal Mapping
- Haberl et al — Spectrotemporal Mapping (the normality factor)
- Kelen/ El-Sherif — Specrtal Turbulance Analysis
- Malek et al — Wavelet decomposition
- Chan — Acceleration Spectrum Analysis

SIGNAL AVERAGED EKG

Frequency domain analysis:
why is is not used more often?

- **It requires complex statistical computations**
- **It is not standardized**
- **Its additional value, with respect to the more established time-domain analysis techniques, has not been fully defined**

Improved diagnostic value of combined time- and frequency-domain analysis for arrhythmic events in 602 post-MI patients



Different SAECG Criteria May Be Required For Different Clinical Settings

- Time-domain criteria for late potentials (RMS40, LAS40) are more predictive of spontaneous and/or inducible sustained monomorphic VT.

- QRS duration criteria are more predictive of malignant arrhythmic events (hypotensive polymorphic VT/VF) in the post-MI period. This has first been shown by the CAST substudy of SAECG (El-Sherif et al, JACC 1995)

THE SIGNAL AVERAGED ECG AS A RISK STRATIFIER OF SCD IN MULTUCENTER CLINICAL TRIALS

- CAST
- CABG-PATCH
- MUSTT
- MADIT-II

Prognostic value of the SAECG after MI (CAST Substudy)

Population: 1211 pts with AMI (CAST criteria) without exclusion criteria based on Holter or LVEF

SA-ECG: Time-domain analysis (QRS, LAS, RMS40 at 25- and 40-Hz filter setting)

Follow-up: 12 months

Arrhythmic events: 44 (41 sudden deaths, 3 non fatal VTs)

El-Sherif et al, JACC 1995

Prognostic value of the SAECG after MI (CAST Substudy)

Variable	Chi^2	Probability
QRSD/25 Hz	32.4	.0000
RMS40/25 Hz	4.1	.0433
LAS/25 Hz	23.8	.0000
QRSD/40 Hz	*37. 1*	*.0000*
RMS40/40 Hz	4.5	.0344
LAS/40Hz	10.3	.0001

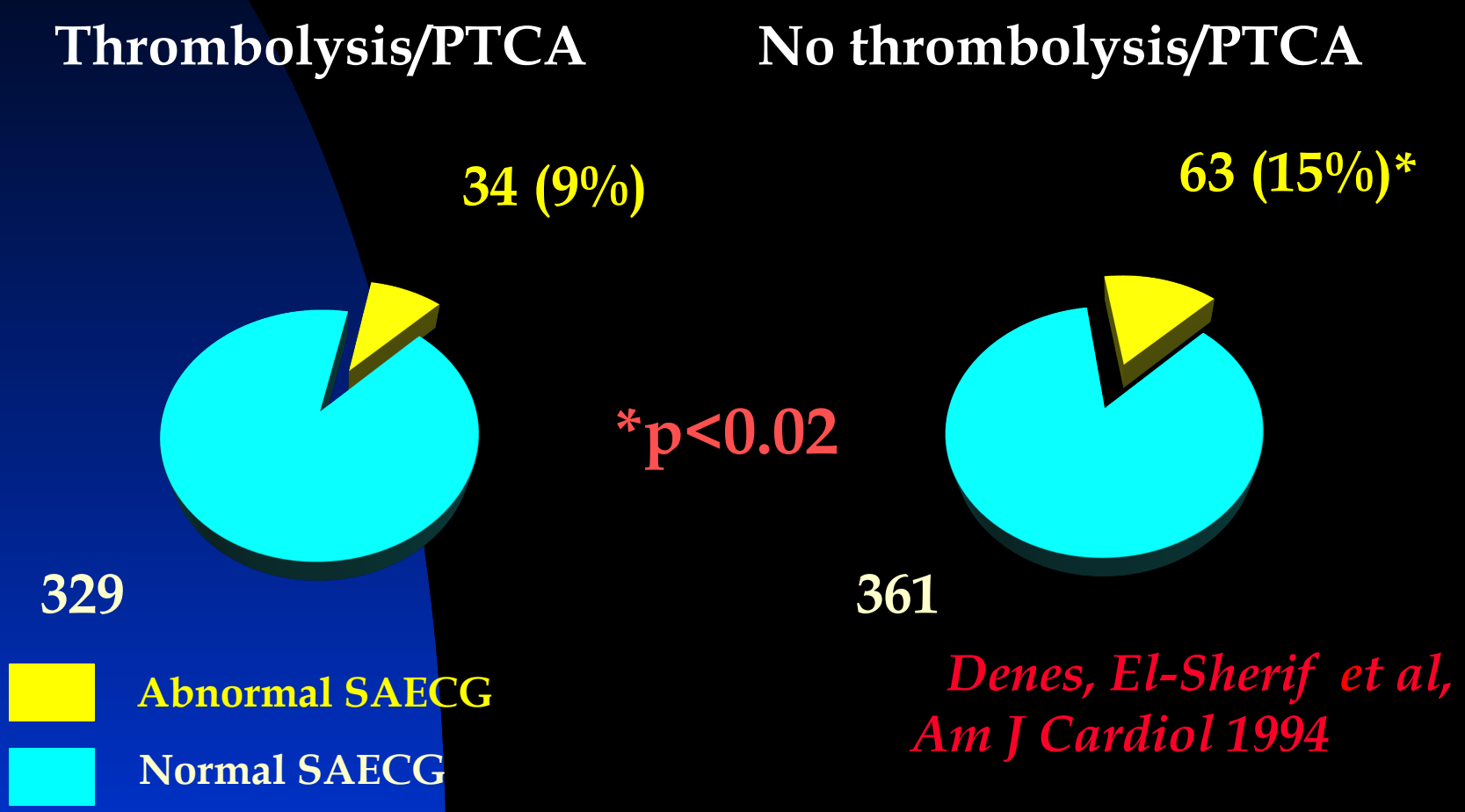
El-Sherif et al, JACC 1995

Time-domain SAECG: prognostic value in post-infarction patients (CAST Substudy)

- **A QRS duration ≥120 msec with a 40-Hz filter was the most statistically significant parameter**
- **In a multivariate analysis, including clinical data, Holter data, LV ejection fraction, and SAECG, an increased QRS duration was the most important predictive factor for arrhythmic events ($p<0.0002$)**

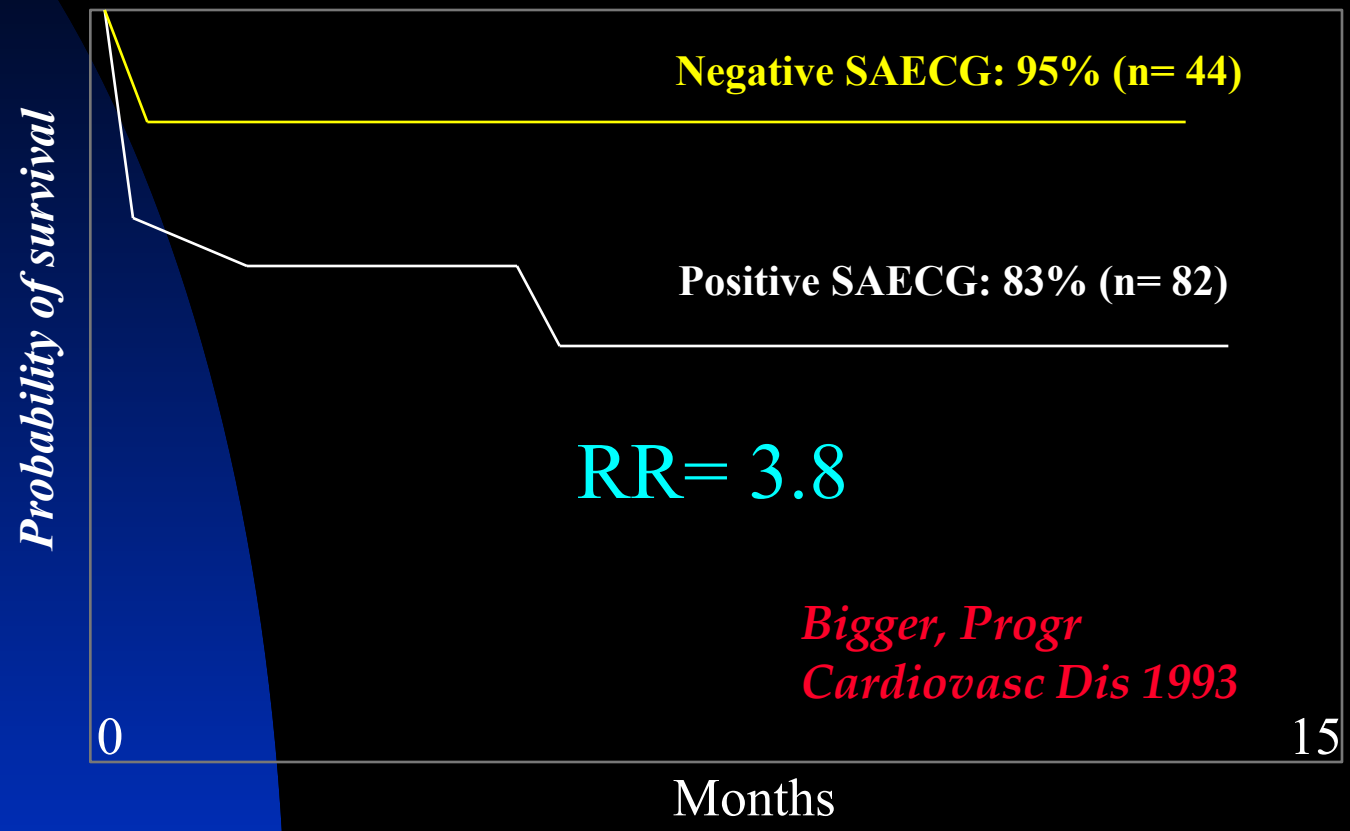
El-Sherif et al, JACC 1995

Prevalence of abnormal SAECG in post-MI pts with or without thrombolysis/PTCA (CAST Substudy)



Denes, El-Sherif et al, Am J Cardiol 1994

Predictive accuracy of the SAECG for death after CABG: the CABG-PATCH pilot study results



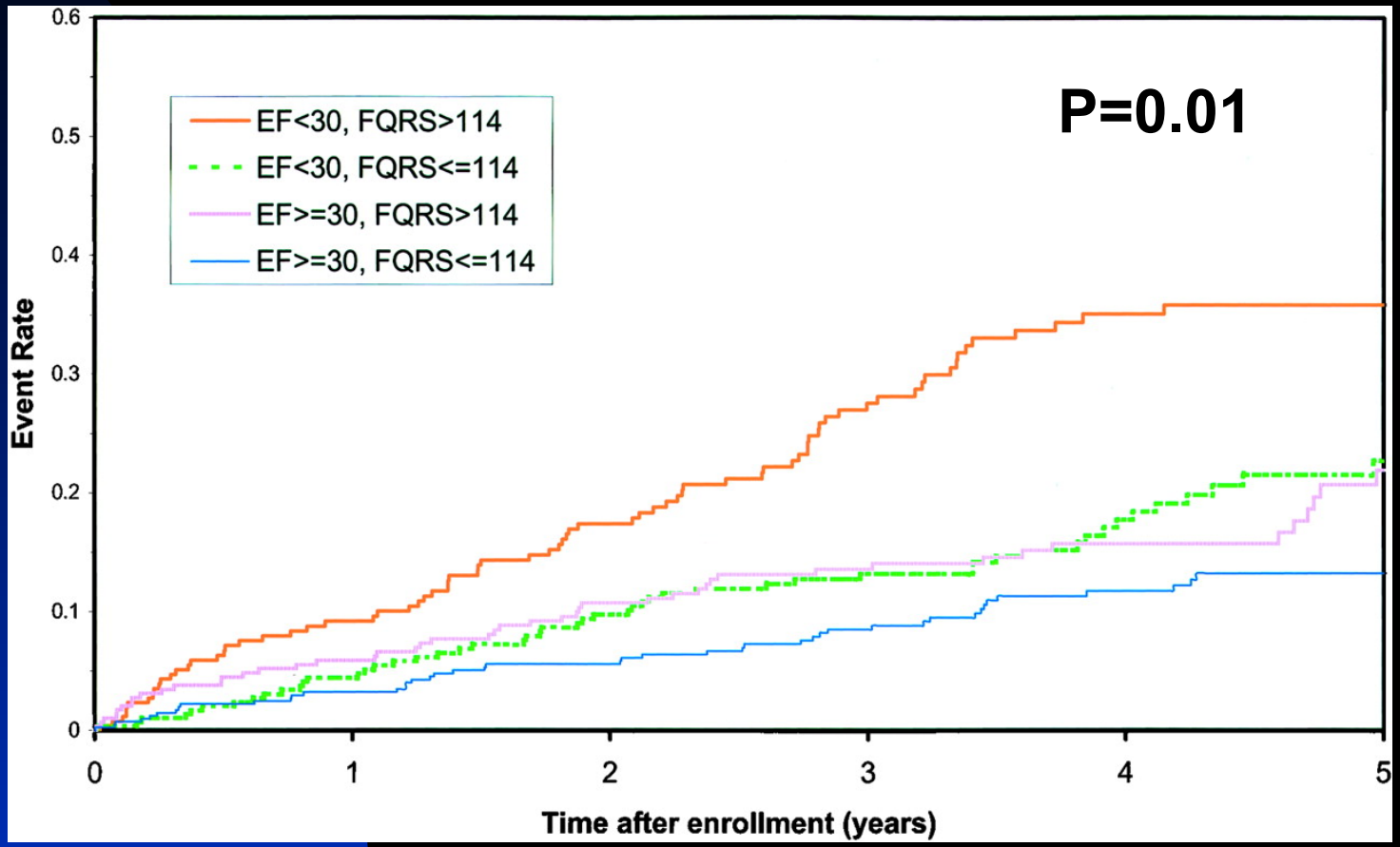
The CABG-PATCH study was based on the encouraging results of its Pilot study. However, the results of the main study was negative

Role of the SAECG in MUSTT

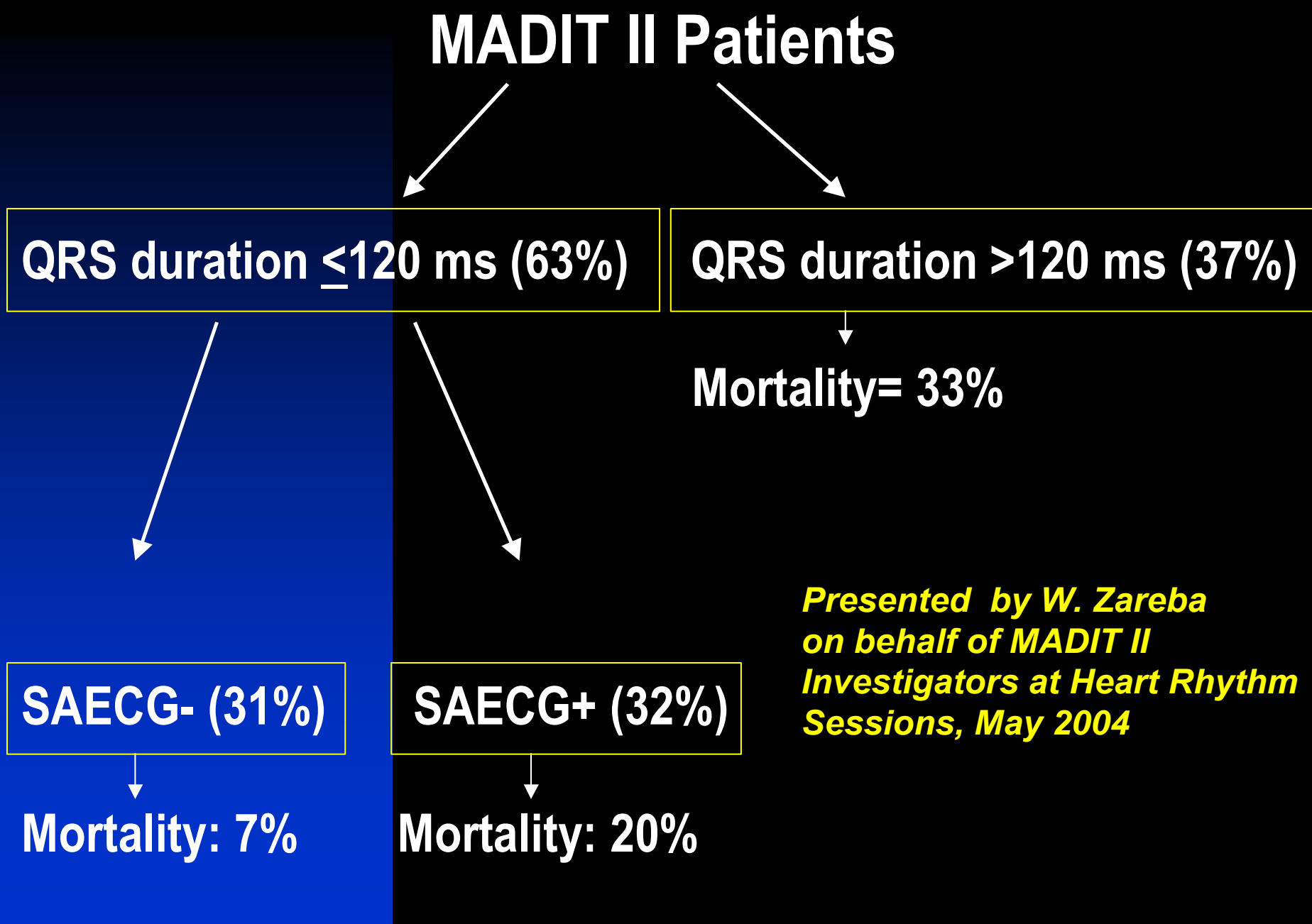
- **An abnormal SAECG (defined as: QRSD>114 ms,RMS40<20 μv at 40-250 Hz) was a strong predictor for both arrhythmic events and total cardiac mortality. "The noninvasive combination of an abnormal SAECG and reduced ejection fraction may have utility in selecting high- risk patients for intervention".**

Gomes JA et al, Circulation 2001

Kaplan-Meier estimates of arrhythmic death or cardiac arrest by SAECG results and ejection fraction in the Multicenter Unsustained Tachycardia Trial (MUSTT)



Gomes JA et al, Circulation 2001


MADIT II Patients
QRS duration ≤120 ms (63%)
QRS duration >120 ms (37%)
Mortality= 33%
SAECG- (31%)
SAECG+ (32%)
Mortality: 7%
Mortality: 20%
Presented by W. Zareba on behalf of MADIT II Investigators at Heart Rhythm Sessions, May 2004

Event-free survival at 400 days stratified by test in pts with known or suspected ventricular arrhythmias

Gold et al, JACC 2000

	Events (n)	Relative Risk	Log-rank P value	Probability of survival Positive	Negative
Arrhythmia Endpoint					
TWA	12	6.14	<0.029	78.8%	96.6%
EPS	15	4.64	<0.009	76.7%	95.0%
SAECG	15	3.43	<0.01	77.5%	93.4%
Arrhythmia Endpoint or Death					
TWA	15	8.03	<0.004	74.1%	96.8%
EPS	19	2.88	<0.038	75.4%	91.5%
SAECG	17	2.52	<0.035	78.4%	91.4%

A comparison of TWA, EPS, and SAECG in this multicenter study showed more or less similar positive and negative predictive power.

Combined assessment of TWA and LPs to predict arrhythmic events after MI Ikeda et al, JACC 2000

"The combination of TWA and LPs was associated with a high predictive accuracy for arrhythmic events after AMI"

	Sens	Spec	+PA	-PA	Total PA	P value
TWA	93%	59%	28%	98%	64%	0.006
LPs	53%	85%	38%	91%	80%	0.0008
EF	60%	78%	32%	92%	75%	0.004
TWA+LPs	53%	91%	50%	92%	85%	0.0001
TWA+EF	60%	84%	39%	92%	80%	0.0005
LPs+EF	40%	86%	33%	89%	79%	0.001
TWA+LPs+EF	40%	91%	43%	90%	83%	0.001

n= 102 cases; PA= predictive accuracy

Prognostic value of the SAECG for arrhythmic events following MI: A meta-analysis

Population:	**4493 pts with AMI from 14 prospective studies**
SA-ECG:	**Within a month of MI**
Follow-up:	**13 months**
Abnl SAECG:	**29%**
Arrhythmic events:	**7%**

Turitto et al, in: Non-invasive Electrocardiology in Clinical Practice. Futura, 2001

Prognostic value of the SAECG for arrhythmic events after MI: A meta-analysis

	MEAN	RANGE
+predictive value:	17%	8-29
- predictive value:	96%	81-99

Turitto et al, in: Non-invasive Electrocardiology in Clinical Practice. Futura, 2001

Prognostic value of the SAECG for arrhythmic events after MI: statistics on 22 studies and 9883 patients (mean follow-up: 22 months)

Follow-up (mos)	22
Arrhythmic events (%)	7.2
Sensitivity (%)	65
Specificity (%)	76
+ predictive accuracy (%)	18
Relative risk	6.9
Odds ratio	12.4

Bailey et al, JACC 2001

Future Status of SAECG as risk stratifier of SCD

- At the present time, reduced LVEF is the main indicator for primary ICD prophylaxis (CMS, 3/05). This position has at least two limitations: one, it is redundant in patients with reduced LVEF who may eventually die from pump failure (at least 50%); two, it ignores patient with more preserved LVEF who may be at risk for SCD.
- The SAECG, in combination with one or more other risk stratifiers, e.g., TWA, markers of autonomic imbalance, biochemical markers, etc, may in the future optimize patients selection for primary ICD prophylaxis. However, prospective data collection either through the registery inspired by the CMS decision in favor of a low LVEF or a new multicenter study (e.g., the M2 Risk study), may be necessary to define the best risk stratification algorithm.

THANK YOU

NABIL EL-SHERIF