Novel Methods to Stratify Arrhythmia Risk Using Digital Electrocardiography

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Professor of Medicine
Stony Brook University Medical Center
Target Population for Risk Stratification

- General adult population
- Multi-risk subgroup
- Any previous coronary event
- EF < 35% or heart failure
- Cardiac-arrest, VF/VT survivors
- High-risk post-MI subgroups

Incidence (%/yr)

Total Events (n/yr)

SCD-HeFT
AVID
CASH
MADIT
MADIT-II Inclusion Criteria

- Q-wave MI ≥ 4 weeks
- LVEF ≤ 0.30
- ≥ 21 years of age; no upper age limitation
- No requirement for NSVT or EPS

MADIT-II Survival Results

<table>
<thead>
<tr>
<th>Year</th>
<th>No. At Risk</th>
<th>Defibrillator</th>
<th>Conventional</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>742</td>
<td>502 (0.91)</td>
<td>329 (0.90)</td>
</tr>
<tr>
<td>1</td>
<td>502 (0.91)</td>
<td>274 (0.94)</td>
<td>170 (0.78)</td>
</tr>
<tr>
<td>2</td>
<td>274 (0.94)</td>
<td>110 (0.78)</td>
<td>65 (0.69)</td>
</tr>
<tr>
<td>3</td>
<td>110 (0.78)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

P = 0.007

SCD-HeFT Inclusion Criteria

- Symptomatic CHF (NYHA Class II and III) due to ischemic or non-ischemic dilated cardiomyopathy
- LVEF ≤ 35%
- ≥ 18 years of age; no upper age limitation
- CHF ≥ 3 months
- On optimal medical therapy for > 3 months
  - Appropriate dose of ACE-I
  - Beta blocker, if tolerated

SCD-HeFT Protocol

DCM + CAD and CHF

EF ≤ 35%

NYHA Class II or III

6-Minute Walk, Holter

R

Placebo N = 847

Amiodarone N = 845

ICD Implant N = 829

2521 Patients

Minimum of 2.5 years follow-up required

45 months average follow-up

Optimized βB, ACE-I, Diuretics

SCD-HeFT Mortality Rate Overall Results

<table>
<thead>
<tr>
<th>Months of Follow-Up</th>
<th>Mortality Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>12</td>
<td>0.1</td>
</tr>
<tr>
<td>24</td>
<td>0.2</td>
</tr>
<tr>
<td>36</td>
<td>0.3</td>
</tr>
<tr>
<td>48</td>
<td>0.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>No. at Risk 1</th>
<th>No. at Risk 2</th>
<th>No. at Risk 3</th>
<th>No. at Risk 4</th>
<th>No. at Risk 5</th>
<th>No. at Risk 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone</td>
<td>845</td>
<td>772</td>
<td>715</td>
<td>484</td>
<td>280</td>
<td>97</td>
</tr>
<tr>
<td>Placebo</td>
<td>847</td>
<td>797</td>
<td>724</td>
<td>505</td>
<td>304</td>
<td>89</td>
</tr>
<tr>
<td>ICD</td>
<td>829</td>
<td>778</td>
<td>733</td>
<td>501</td>
<td>304</td>
<td>103</td>
</tr>
</tbody>
</table>

Hazard Ratio (97.5% CI) P-Value
- Amiodarone vs. Placebo: 1.06 (0.86 - 1.30) 0.53
- ICD vs. Placebo: 0.77 (0.62 - 0.96) 0.007

Why Not Implant an ICD?

- Cost considerations
- Inappropriate shocks
- Recalls of pulse generators and leads
- Implant-related complications
- Minority of patients in MADIT-II and SCD-HeFT received appropriate shocks
  - Risk stratification needed to identify low risk patients that may not require ICDs
Risk Stratification Methods

• T wave alternans

• Holter-based methods
  – Heart rate variability
  – Heart rate turbulence
  – QT variability (QT length)
  – T wave variability (T wave amplitude)
  – Signal-averaged ECG
Electrical Alternans Preceding Ventricular Fibrillation
T-Wave Alternans Measurement: Spectral Method

ECG

TIME SERIES

SPECTRUM

T Wave Level (µV)

Beat Number

128 Beats

Spectrum (µV²)

Frequency (Cycles/Beat)

Resp

Pedaling

Alternans

FFT
Heart Rate

T-Wave Alternans

Negative

Positive

Heart Rate

T-Wave Alternans
RELATION BETWEEN ECG AND ACTION POTENTIAL

Mechanism Linking TWA to Ventricular Arrhythmias

Action Potential Alternans Leads to T-Wave Alternans

Spatially Discordant Alternans Leads to Dispersion of Recovery, Wave Front Fractionation, and Reentry
University of Maryland ICM Study

- Prospective evaluation of 251 patients
- Inclusion Criteria
  - Documented CAD
  - LVEF ≤ 0.40
  - Normal Sinus Rhythm
  - Indication for EPS
- Exclusion Criteria
  - Atrial fibrillation or frequent ectopy
  - Antiarrhythmic drug use at time of study

Rashba et. al., JCE 2002; 13: 845-850
TWA Testing Modality

- Choice of testing modality was determined by exercise capacity as well as patient and physician preference, since exercise and pacing were reported previously to yield concordant results.

- Testing modality
  - Exercise only \( (n=72) \)
  - Pacing only \( (n=107) \)
  - Both tests \( (n=71) \)
# Patient Population

<table>
<thead>
<tr>
<th></th>
<th>Pacing</th>
<th>Exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (yrs)</strong></td>
<td>66 ± 11</td>
<td>64 ± 10</td>
</tr>
<tr>
<td><strong>Male (%)</strong></td>
<td>81</td>
<td>79</td>
</tr>
<tr>
<td><strong>Mean EF (%)</strong></td>
<td>26 ± 8</td>
<td>28 ± 8</td>
</tr>
<tr>
<td><strong>NYHA II/III (%)</strong></td>
<td>88</td>
<td>92</td>
</tr>
<tr>
<td><strong>ICD (%)</strong></td>
<td>68</td>
<td>71</td>
</tr>
<tr>
<td><strong>Outcome event (%)</strong></td>
<td>35</td>
<td>35</td>
</tr>
</tbody>
</table>

*p = NS for all comparisons*
## Comparison of Exercise and Pacing TWA

<table>
<thead>
<tr>
<th>TWA Results</th>
<th>Pacing (n=178)</th>
<th>Exercise (n=143)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive (%)</td>
<td>65</td>
<td>49</td>
</tr>
<tr>
<td>Negative (%)</td>
<td>27</td>
<td>26</td>
</tr>
<tr>
<td>Indeterminate (%)</td>
<td>8</td>
<td>25</td>
</tr>
</tbody>
</table>

* p < 0.001
Clinical Follow-up

- Mean follow-up 499 ± 395 days
- There were 88 events (35% of pts)
  - Appropriate ICD therapy 50
  - VT/VF 2
  - Death 35
  - Cardiac arrest 1
Exercise TWA Prediction of Endpoints

![Graph showing event-free survival over years with hazard ratio (HR) and p-value.](image)

- **HR** = 2.2
- **p** = 0.03
Pacing TWA Prediction of Endpoints

\[ p = \text{NS} \]
Effects of selective autonomic blockade on TWA
Methods

- Prospective evaluation of 74 patients with inducible SMMVT
- 14 pts excluded due to indeterminate TWA tests
- TWA measured after completion of EPS by spectral method (Cambridge Heart Inc.)
- Oral beta blockers withheld > 24 hours
- TWA measured during atrial pacing (100, 109, 120 bpm) at baseline and following infusion of either atropine (n=20), esmolol (n=20), or no drug (n=20, control)

Rashba et. al., Circulation 2002; 105: 837-42
Baseline

Esmolol
Predictive Value of TWA (QRS < 120 ms)

Event-free Survival

Years

HR = 5.8
p = 0.02
Predictive Value of TWA (QRS ≥ 120 ms)

Event-free Survival

Years

p = NS
Prognostic value of TWA

HR = 2.2
p = 0.03

<table>
<thead>
<tr>
<th>No. At Risk</th>
<th>TWA-</th>
<th>TWA+</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>38</td>
<td>70</td>
</tr>
<tr>
<td>.5</td>
<td>31</td>
<td>55</td>
</tr>
<tr>
<td>1</td>
<td>26</td>
<td>41</td>
</tr>
<tr>
<td>1.5</td>
<td>22</td>
<td>26</td>
</tr>
<tr>
<td>2</td>
<td>18</td>
<td>20</td>
</tr>
</tbody>
</table>
TWA, if LVEF 30-40%
TWA, if LVEF < 30%
EPS, if TWA+

- EPS+
- EPS-

Event-free Survival

Years

No. At Risk
EPS- 15 12 9 6 4
EPS+ 55 43 33 21 17

p = NS
EPS, if TWA- and LVEF < 30 or IND TWA

HR = 4.7
p = 0.015

No. At Risk
EPS- 18 16 16 13 11
EPS+ 36 21 14 12 9
TWA in CHF

Bloomfield et. al. JACC 2006; 47: 456-63
Is TWA Testing All That We Need?

- Patients excluded from TWA testing:
  - Atrial fibrillation (20-30% of CHF pts)
  - Poor functional capacity
- Ineligibility or inability to complete TWA testing may identify high risk patients
- Extending ICD indications to broader population (EF 35-45%) may require multiple tests to achieve sufficient PPV
- Digital Holter applicable to more patients
Preserved HRV Identifies Low Risk Nonischemic Cardiomyopathy Patients: Results from the DEFINITE Trial

Eric J. Rashba, N.A. Mark Estes, Paul Wang, Andi Schaechter, Adam Howard, Wojciech Zareba, Jean-Philippe Couderc, Juha Perkiomaki, Joseph Levine, and Alan Kadish for the DEFINITE Investigators

Funded by NIH K23 HL67198
Kaplan-Meier Estimates of Death from Any Cause (Panel A) and Sudden Death from Arrhythmia (Panel B) among Patients Who Received Standard Therapy and Those Who Received an Implantable Cardioverter-Defibrillator (ICD)

**DEFINITE HRV Substudy**

- **Hypothesis:** Low-risk pts with preserved HRV may not require an ICD
- **First DEFINITE pt enrolled:** July 9, 1998
- **Digital Holter equipment obtained:** August 1999 (Burdick 6632)
- **24-hour Holter obtained:** at baseline or at earliest possible follow-up visit
Methods

• Manual editing to exclude ectopy/noise
• SDNN = primary HRV variable
• Pre-specified analytic plan:
  – SDNN data split into tertiles, pts with AF or frequent ectopy (>25% of beats) analyzed in a separate group
Methods (2)

- Clinical characteristics of enrolled and excluded pts compared using unpaired t tests, Chi square test
- Kaplan-Meier analysis to examine relation of SDNN with outcome
- Events committee unaware of treatment assignment
- Endpoints:
  - All cause mortality
  - Cardiac mortality
  - Sudden death + appropriate ICD shocks
  - Appropriate ICD shocks
Results

• 303/458 patients enrolled
• 31/40 enrolling centers participated
• 29 pts excluded (<18 hours analyzable data)
• AF present in 16%, frequent ectopy 7%
• Timing of Holter after randomization
  – < 3 months 42% of patients, mean 7 ± 10 months
  – F/U for outcome analyses starting at Holter date
## Clinical Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Holter (n=274)</th>
<th>No Holter (n=184)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>59 ± 12</td>
<td>58 ± 13</td>
</tr>
<tr>
<td>Male gender</td>
<td>199 (73%)</td>
<td>127 (69%)</td>
</tr>
<tr>
<td>Non-white *</td>
<td>56 (22%)</td>
<td>62 (36%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>64 (23%)</td>
<td>41 (22%)</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>21 ± 6</td>
<td>22 ± 6</td>
</tr>
</tbody>
</table>

* p < 0.05
# Clinical Characteristics

<table>
<thead>
<tr>
<th>NYHA Class</th>
<th>Holter (n=274)</th>
<th>No Holter (n=184)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>71 (26%)</td>
<td>28 (15%)</td>
</tr>
<tr>
<td>II</td>
<td>149 (54%)</td>
<td>114 (62%)</td>
</tr>
<tr>
<td>III</td>
<td>54 (20%)</td>
<td>41 (22%)</td>
</tr>
</tbody>
</table>

* p < 0.05
## Cardiovascular Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Holter (n=274)</th>
<th>No Holter (n=184)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitor</td>
<td>235 (86%)</td>
<td>157 (85%)</td>
</tr>
<tr>
<td>ARB</td>
<td>31 (11%)</td>
<td>20 (11%)</td>
</tr>
<tr>
<td>Beta Blockers *</td>
<td>245 (89%)</td>
<td>144 (78%)</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>14 (5%)</td>
<td>9 (5%)</td>
</tr>
</tbody>
</table>

* p < 0.05
## Clinical Outcome

<table>
<thead>
<tr>
<th></th>
<th>Holter (n=274)</th>
<th>No Holter (n=184)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total mortality *</td>
<td>26 (9%)</td>
<td>42 (23%)</td>
</tr>
<tr>
<td>Sudden cardiac</td>
<td>4 (2%)</td>
<td>13 (7%)</td>
</tr>
<tr>
<td>Cardiac, not sudden</td>
<td>10 (4%)</td>
<td>11 (6%)</td>
</tr>
<tr>
<td>Non-cardiac</td>
<td>12 (4%)</td>
<td>14 (8%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>0 (0%)</td>
<td>4 (2%)</td>
</tr>
<tr>
<td>ICD shocks</td>
<td>22 (15%)</td>
<td>13 (16%)</td>
</tr>
</tbody>
</table>

* p < 0.05
Total Mortality (ICD + STD)

Cardiac Mortality (ICD + STD)

Event-free survival

Years

P=0.006
SCD + ICD shocks (ICD + STD)

P = 0.06
Appropriate ICD shocks

Event-free survival

Years

P=0.10
Limitations

• Substudy pts were at lower risk than pts who did not have a Holter
• Holters not performed at enrollment in all pts
• Missed events before Holter could be performed, especially in STD therapy patients
• Favorable risk profile of substudy patients facilitates identification of low risk pts
Conclusions

• NIDCM pts with preserved HRV are at low risk for cardiac events
• NIDCM pts excluded from HRV analysis due to AF/PVCs are at high risk
• Prospective verification of these findings required before considering withholding ICD therapy from NIDCM patients
Electrophysiological Effects of Late PCI After MI:
The OAT-EP Trial

Eric J. Rashba, Judith S. Hochman, Jean-Philippe Couderc, Gervasio A. Lamas, Sharri M. Hollist, Vladimir Dzavik, Warren Cantor, Carlos Vozzi, Christopher Buller, Sandra Forman, Lisa Aronson Friedman, John R. Ross, Antonio Carlos Carvalho on behalf of the OAT-EP Investigators
Rationale for Late Reperfusion

- Late open artery hypothesis suggests that PCI of occluded IRAs after the acute phase of MI would improve prognosis
- Mechanisms of potential benefit
  - Recruitment of hibernating myocardium
  - Prevention of LV enlargement
  - Source for collateral flow
- **Stabilization of electrical substrate**
  - Limited data suggest association between patent IRA and improved HRV, SAECG and QT interval dispersion
  - No data available from large randomized controlled trials
OCCLUDED ARTERY TRIAL

Day 3-28 post MI  Stable

Occluded IRA

Increased long-term risk

PCI/Stent + Medical Rx

Medical Rx alone

Primary Endpoint:
Death, MI, NYHA Class IV heart failure over an average 3-year follow-up
OAT Eligibility

Confirmed Index MI + Total IRA Occlusion + High Risk

Confirmed by 2 out of 3
1. Ischemic symptoms ≥ 30 minutes
2. Elevated cardiac markers
3. EKG criteria: STEMI or NSTEMI, Q or Non Q wave MI

TIMI Flow 0 or 1 in IRA
3-28 days post MI

EF <50%
and/or
Proximal Occlusion of a major epicardial vessel supplying >25% LV

Major Exclusion Criteria

- Significant left main or 3 vessel CAD
- Hemodynamic or electrical instability
- Rest or low-threshold angina
- NYHA Class III-IV HF or shock
OAT Study Results

- Sustained IRA patency at 1 year in 83% of PCI patients vs 25% Med Rx (TOSCA-2 ancillary study)
- Baseline SPECT: moderately preserved infarct zone viability in 69% of 124 pts (OAT-NUC ancillary study)
- No effect on composite endpoint of death, MI or NYHA Class IV CHF (OAT Trial)
OAT-EP Study Aims

• **Primary Aim**
  – Characterize effects of late PCI on the autonomic nervous system (HRV)
    • $\alpha_1$ nonlinear HRV, superior prognostic value in post MI patients with LV dysfunction (Huikuri Circulation 2000; 101: 47-53)
    • Primary endpoint: change in $\alpha_1$ from baseline to 1 year

• **Secondary Aims**
  – Characterize effects of late PCI on
    • Impulse conduction (SAECG)
      – fQRS potent predictor of mortality (MUSTT)
    • Ventricular repolarization (TWV)
      – Beat-to-beat variability in T wave morphology
      – Independent predictor of arrhythmic events in MADIT-2
    • Secondary endpoints: change in fQRS and TWV from baseline to 1 year
Kaplan-Meier estimates of arrhythmic death or cardiac arrest by SAECG result

OAT-EP Study Design

• Must meet all OAT eligibility criteria

• Normal sinus rhythm
  – HRV and TWV measurement

• Narrow QRS (<120 ms)
  – SAECG measurement
OAT-EP Methods

- Ten minute digital Holter prior to randomization and at one year
- Data acquired at 1000 Hz using Burdick 92510 digital Holter recorder
- All data centrally analyzed at core lab
- SAECGs excluded if noise > 1 µV
- Excluded from TWV analysis if HR unstable, excessive ectopy or noise
Enrolled between April 2003 and December 2005

Enrolled in OAT-EP
N=300

36 of 217 OAT sites

Randomized to PCI
N=151

Lost to follow-up N=11
Died N=8
BL or 1 year data unusable N=14

Paired data for ∆α 1 year-BL
N=118
78%

Paired data for ∆TWV 1 year-BL
N=104
69%

Paired data for ∆fQRS 1 year-BL
N=90
57%

Randomized to MED
N=149

Lost to follow-up N=13
Died N=4
BL or 1 year data unusable N=15

Paired data for ∆α 1 year-BL
N=117

Paired data for ∆TWV 1 year-BL
N=103

Paired data for ∆fQRS 1 year-BL
N=80
Statistical Considerations

- Power based on actual numbers of analyzable pairs
  - Primary endpoint: change in $\alpha_1$ (HRV)
    - 80% to detect a difference between groups of 0.1
  - Secondary endpoint: change in fQRS (SAECG)
    - 99% power to detect a difference of 10 ms
    - 80% power to detect a difference of 5.5 ms
  - Secondary endpoint – change in TWV
    - 91% power to detect a difference of 10 $\mu$V
    - 80% power to detect a difference of 8 $\mu$V
- $p < 0.05$ required for statistical significance
## Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>PCI (N=151)</th>
<th>MED (N=149)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age mean ± SD, years</td>
<td>57.6±10.5</td>
<td>57.2±10.5</td>
</tr>
<tr>
<td>Male *</td>
<td>74.5</td>
<td>84.1</td>
</tr>
<tr>
<td>Prior angina</td>
<td>18.8</td>
<td>19.9</td>
</tr>
<tr>
<td>Prior MI</td>
<td>6.7</td>
<td>6.6</td>
</tr>
<tr>
<td>Diabetes *</td>
<td>14.8</td>
<td>26.5</td>
</tr>
<tr>
<td>NYHA Class I at the time of randomization</td>
<td>84.6</td>
<td>80.8</td>
</tr>
<tr>
<td>EKG - ST elevation or Q-wave or R-wave loss</td>
<td>88.6</td>
<td>88.7</td>
</tr>
<tr>
<td>Thrombolytic therapy for index MI</td>
<td>13.4</td>
<td>14.6</td>
</tr>
<tr>
<td>Days from MI to randomization Median (25.75%)</td>
<td>11 (6, 20)</td>
<td>12 (6,21)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>54.4</td>
<td>62.3</td>
</tr>
<tr>
<td>Caucasian Race</td>
<td>77.2</td>
<td>77.5</td>
</tr>
</tbody>
</table>

* p<0.05
Angiographic Characteristics

<table>
<thead>
<tr>
<th></th>
<th>PCI</th>
<th>MED</th>
</tr>
</thead>
<tbody>
<tr>
<td>IRA</td>
<td>75</td>
<td>80</td>
</tr>
<tr>
<td>TIMI 0</td>
<td>20</td>
<td>29</td>
</tr>
<tr>
<td>Multivessel</td>
<td>13</td>
<td>15</td>
</tr>
<tr>
<td>Mean</td>
<td>47.9</td>
<td>47.7</td>
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</table>
# Medical Therapy

<table>
<thead>
<tr>
<th>Agent</th>
<th>Baseline</th>
<th>1-Year</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>PCI (N=149)</td>
<td>MED (N=149)</td>
</tr>
<tr>
<td>ACE Inhibitor</td>
<td>80.5</td>
<td>81.2</td>
</tr>
<tr>
<td>Angiotensin Receptor Blocker</td>
<td>3.4</td>
<td>2.0</td>
</tr>
<tr>
<td>β-Blocker</td>
<td>89.3</td>
<td>92.6</td>
</tr>
<tr>
<td>Calcium Channel Blocker</td>
<td>5.4</td>
<td>7.4</td>
</tr>
<tr>
<td>Diuretic</td>
<td>16.1</td>
<td>20.1</td>
</tr>
<tr>
<td>Anti-arrhythmics</td>
<td>1.3</td>
<td>2.7</td>
</tr>
</tbody>
</table>
Changes in $\alpha_1$

- PCI: $p=0.38$
- MED: $p=0.29$

Baseline vs. 1-Year:
- PCI: $+0.01\pm0.34$
- MED: $-0.03\pm0.32$
Changes in fQRS

- PCI group: 1±12ms vs. 4±12ms
  - p=0.25

- MED group: 1±12ms vs. 4±12ms
  - p=0.27
  - p=0.01
Changes in TWV

 PCI vs. MED

Baseline: -6±25 vs. -3±31

p = 0.46

p = 0.01

p = 0.27
### INDEPENDENT PREDICTORS OF CHANGE IN $\alpha_1$

<table>
<thead>
<tr>
<th>Variable</th>
<th>Direction of Effect</th>
<th>P Value</th>
</tr>
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<tbody>
<tr>
<td>PCI Group</td>
<td>—</td>
<td>0.52</td>
</tr>
<tr>
<td>$\beta$-Blockers at 1 year</td>
<td>↓</td>
<td>0.03</td>
</tr>
<tr>
<td>Male</td>
<td>↓</td>
<td>0.04</td>
</tr>
<tr>
<td>Ejection Fraction</td>
<td>↓</td>
<td>0.04</td>
</tr>
</tbody>
</table>
## INDEPENDENT PREDICTORS OF CHANGE IN fQRS

<table>
<thead>
<tr>
<th>Variable</th>
<th>Direction of Effect</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCI Group</td>
<td>—</td>
<td>0.14</td>
</tr>
<tr>
<td>Prior MI</td>
<td>↓</td>
<td>0.01</td>
</tr>
<tr>
<td>Hypertension</td>
<td>↓</td>
<td>0.03</td>
</tr>
<tr>
<td>ACEI at Baseline</td>
<td>↑</td>
<td>0.05</td>
</tr>
</tbody>
</table>
# Independent Predictors of Change in TWV

<table>
<thead>
<tr>
<th>Variable</th>
<th>Direction of Effect</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCI Group</td>
<td>—</td>
<td>0.38</td>
</tr>
<tr>
<td>Age</td>
<td>↑↑</td>
<td>0.04</td>
</tr>
<tr>
<td>Multivessel Disease</td>
<td>↓↓↓</td>
<td>0.06</td>
</tr>
<tr>
<td>Thrombolytics</td>
<td>↑↑</td>
<td>0.02</td>
</tr>
<tr>
<td>EKG - ST elevation or Q-wave or R-wave loss</td>
<td>↓↓</td>
<td>0.09</td>
</tr>
</tbody>
</table>
Conclusion

Despite:

- Excellent 1-year patency after PCI
- Retained viability

**PCI did not reduce markers of arrhythmia vulnerability**

- No effect on
  - autonomic nervous system (HRV)
  - ventricular repolarization (TWV)
  - impulse conduction (SAECG)
Limitations of Holter-based methods

- Exclusion of ~33% of patients
- Validated cutpoints for abnormal results not available for all tests
- Automated data processing and test interpretation not available
Goals of Risk Stratification

• Exclude low risk SCD-HeFT patients
  – TWA may not be as good as advertised
  – Annual reassessment mandatory
  – Multiple tests for sufficient NPV

• Identify new candidates for prophylactic ICD
  (e.g. LVEF 35-45%)
  – TWA insufficient
  – Multiple tests for sufficient PPV