**Showcasing MHIF Research**

3 PRESENTATIONS

2 PANELS

17 POSTERS

**Presentations Sharing MHIF Research:**

- **Show and Tell with the Experts: SCAD & MINOCA Cases in the Cath Lab**
  Emmanouil Brilakis, MD
  Sun., Nov. 17

- **Complex and High Risk Interventions: Optimal Approach to Chronic Total Occlusions**
  Emmanouil Brilakis, MD
  Sun., Nov. 17

- **International Cases: Show & Tell from the Cath Lab - Challenging Coronary Cases**
  Emmanouil Brilakis, MD
  Mon., Nov. 18

**Panels:**

**What’s New in the Guidelines: Updates and Controversies**
Steven Bradley, MD - Moderator
Sun., Nov. 17

**Meet, Greet and Learn from the Masters in Interventional Cardiology**
Panel: Table on Approach to Treatment of the Lesion
Emmanouil Brilakis, MD – Panelist
Sat. Nov. 16
Minneapolis Heart Institute Foundation® Cardiovascular Grand Rounds

Title: AHA Scientific Sessions - Preview

Speakers:

- Circadian Dependence of Microvascular Obstruction in ST-elevation Myocardial Infarction
  Nicole Bonfig, BS, Research Assistant, Minneapolis Heart Institute Foundation®

- Impact of Left Atrial Pressure on Long-Term Outcomes in Patients with Mitraclip Therapy
  Hiroki Niikura, MD, Research Scholar, Valve Science Center Minneapolis Heart Institute Foundation®

- A Phase 1, First-in-man Trial of Percutaneous Delivery of a Porcine-derived Extracellular Matrix Hydrogel Following St-elevation Myocardial Infarction
  Jay Traverse, MD, Cardiologist, Minneapolis Heart Institute®, Abbott Northwestern Hospital

- Temporal Changes of Noninvasive Electrocardiographic Risk Factors for Sudden Cardiac Death in Post-Myocardial Infarction Patients with Preserved Ejection Fraction: Insights from PRESERVE-EF
  Iosif Xenogiannis, MD, Research Scholar, Minneapolis Heart Institute Foundation®

Date: November 11, 2019
Time: 7:00 - 8:00 AM
Location: Minneapolis Heart Institute Foundation, Suite 100, Learning Center

OBJECTIVES
At the completion of this activity, the participants should be able to:
1. Summarize emerging research that colleagues will present at upcoming national scientific meeting.
2. Synthesize ideas and input from across disciplines relevant to each presentation.
3. Recommend content revisions or areas of focus to the presenters.

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### MHIF Research: AHA HIGHLIGHTS NOVEMBER 2019

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#### PRESENTATIONS SHARING MHIF RESEARCH:

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### Circadian Dependence of Microvascular Obstruction

Nicole Bonfig, BS
Circadian Pattern of Microvascular Obstruction: Background

- MVO occurs frequently following STEMI (50%)
- Circadian pattern remains elusive
- MVO may result from distal embolization or extrinsic compression of the microcirculation
  - Myocardial edema from ischemia and reperfusion injury.
- Risks: Adverse left-ventricular remodeling, heart failure, rehospitalization and increased mortality.
- Greater ischemic times and greater infarct size.

Circadian Pattern of Microvascular Obstruction: Methods

Subjects taken from TIME and PCII datasets
Subjects taken from the overall level 1 database
Patients excluded where medical record could not be obtained
MVO occurred
No MVO occurred
Circadian Pattern of Microvascular Obstruction: Results

![Graph showing MVO (n=234) and No MVO (n=175) over time]

Circadian Pattern of Microvascular Obstruction: Results

![Graph showing Average MVO mass vs onset time]

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Circadian Pattern of Microvascular Obstruction: Results

![Graph showing the relationship between MVO Mass and Infarct Size.](image)

\[y = 0.534x + 15.077\]

Circadian Pattern of Microvascular Obstruction: Results

![Graph showing the relationship between MVO Mass and LV Mass.](image)

\[y = 1.502x + 137.36\]
Circadian Pattern of Microvascular Obstruction: Conclusions

- Novel: Among STEMI patients with MVO there was a Circadian distribution peaking in between 6 and 9 AM
  - Gives insight into further study of MVO
- Increase in MVO mass associated with increased infarct size
- Novel: MVO mass increases with increasing LV mass
  - Infarct size larger with increase LV mass

Acknowledgements

Dr. Traverse (PI)
Chase Soukup, 2019 intern
MHIF staff and intern program coordinators
Impact of Left Atrial Pressure on Long-term Outcomes in Patients Treated with Transcatheter Mitral Repair

Hiroki Niikura, MD
Research scholar
Valve Science Center at the Minneapolis Heart Institute Foundation, Abbott Northwestern Hospital

Background

- Major goal for MitraClip is to reduce volume overload in the cardiac chamber.
- Acute MR reduction has been linked to long-term outcomes after MitraClip.

Post-procedural residual MR and outcomes

Sorajja P, et al. JACC. 2017
**Background**

- Post-procedural echocardiographic evaluation of residual MR is challenging.
- The orifices and multiple residual MR jets are appeared following MitraClip deployment.

**Background and object**

- Measurement of left atrial pressure (LAP) monitoring has been proposed for further assessing procedural success.
- LAP directly reflects volume status and is known to be associated with outcomes among heart failure patients.

We examined the impact of the LAP measurement on long-term clinical outcomes following MitraClip therapy.
Study workflow

249 consecutive MR patients who underwent MitraClip therapy from 2012 to 2017 at MHI

N= 64 excluded patients;
• Procedure unsuccess (i.e., unable clip deployment or post-procedural MR of grade 3+ or more) (n=19)
• Incomplete of procedural invasive hemodynamic assessment (n=39)
• In-hospital death (n=6)

A total of 185 patients who underwent pre/post procedural invasive hemodynamic assessment

Patients were grouped using 3 different classifications according to procedural hemodynamics results

Classification No.1; Mean LAP (mLAP) groups;
< 15 mmHg (n=72)
15 to 20 mmHg (n=87)
> 20 mmHg (n=46)

Classification No.2; Peak v-wave LAP (vLAP) groups;
< 25 mmHg (n=93)
25 to 35 mmHg (n=70)
> 35 mmHg (n=22)

Classification No.3; Change in the v LAP (vs. baseline) groups;
Decrease > 15 mmHg (n=56)
5 to 15 mmHg (n=68)
< 5 mmHg (n=61)

Methods

Primary outcomes;

➢ One-year all-cause mortality.
➢ Hospitalization for heart failure at one-year follow-up.
➢ Combined endpoint of all-cause death, hospitalization for heart failure at one-year follow-up.
Comparison of NYHA class at one-year according to mLAP classification

<table>
<thead>
<tr>
<th>mLAP</th>
<th>NYHA class I</th>
<th>class II</th>
<th>class III</th>
<th>class IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;15 mmHg</td>
<td>11.8%</td>
<td>51.5%</td>
<td>36.8%</td>
<td>0.0%</td>
</tr>
<tr>
<td>15 to 20 mmHg</td>
<td>26.8%</td>
<td>41.1%</td>
<td>30.4%</td>
<td>1.8%</td>
</tr>
<tr>
<td>&gt;20 mmHg</td>
<td>17.5%</td>
<td>47.5%</td>
<td>32.5%</td>
<td>2.5%</td>
</tr>
</tbody>
</table>

The frequency of NYHA class III/IV: p=0.063

Comparison of NYHA class at one-year according to vLAP classification

<table>
<thead>
<tr>
<th>vLAP</th>
<th>NYHA class I</th>
<th>class II</th>
<th>class III</th>
<th>class IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;25 mmHg</td>
<td>16.0%</td>
<td>56.8%</td>
<td>25.9%</td>
<td>1.2%</td>
</tr>
<tr>
<td>25 to 35 mmHg</td>
<td>24.2%</td>
<td>38.7%</td>
<td>37.1%</td>
<td>0.0%</td>
</tr>
<tr>
<td>&gt;35 mmHg</td>
<td>9.5%</td>
<td>33.3%</td>
<td>52.4%</td>
<td>4.8%</td>
</tr>
</tbody>
</table>

The frequency of NYHA class III/IV: p=0.48
Comparison of NYHA class at one-year according to change in vLAP classification

<table>
<thead>
<tr>
<th>Decrease vLAP &gt;15 mmHg</th>
<th>5 to 15 mmHg</th>
<th>&lt;5 mmHg</th>
<th>The frequency of NYHA class III/IV p=0.71</th>
</tr>
</thead>
<tbody>
<tr>
<td>NYHA class I</td>
<td>0%</td>
<td>0.0%</td>
<td>35.1%</td>
</tr>
<tr>
<td>class II</td>
<td>15.7%</td>
<td>49.0%</td>
<td>21.1%</td>
</tr>
<tr>
<td>class III</td>
<td>47.4%</td>
<td>44.6%</td>
<td>17.9%</td>
</tr>
<tr>
<td>class IV</td>
<td>31.6%</td>
<td>33.9%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

Kaplan-Meier curve in mLAP groups

- All-cause death: Log-rank test: p=0.12
- Death and HF rehospitalization: Log-rank test: p=0.086
### Kaplan-Meier curve in vLAP groups

#### All-cause death

**Log-rank test: p=0.54**

- final vLAP < 25 mmHg
- 25 to 35 mmHg
- > 35 mmHg

#### Death and HF rehospitalization

**Log-rank test: p=0.41**

- Survival free from all-cause mortality (%)
- Freedom from death or heart failure rehospitalization (%)

Days since procedure

### Kaplan-Meier curve in change in vLAP groups

#### All-cause death

**Log-rank test: p=0.24**

- decrease in vLAP > 15 mmHg
- 5 to 15 mmHg
- < 5 mmHg

#### Death and HF rehospitalization

**Log-rank test: p=0.67**

- Survival free from all-cause mortality (%)
- Freedom from death or heart failure rehospitalization (%)

Days since procedure
Kaplan-Meier curve for freedom from death or HF rehospitalization in patients with residual MR grade 0/1 (n=103)

Log-rank test: p=0.39
- : final mean LAP < 15 mmHg
- : 15 to 20 mmHg
- : > 20 mmHg

Log-rank test: p=0.38
- : final v LAP < 25 mmHg
- : 25 to 35 mmHg
- : > 35 mmHg

Log-rank test: p=0.65
- : decrease in v LAP > 15 mmHg
- : 5 to 15 mmHg
- : < 5 mmHg

Parameters associated with one-year all-cause mortality

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Univariable HR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>One year all-cause mortality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>mLAP ≥ 15 mmHg</td>
<td>2.95 (0.99-8.76)</td>
<td>0.052</td>
</tr>
<tr>
<td>vLAP ≥ 25 mmHg</td>
<td>0.76 (0.32-1.81)</td>
<td>0.54</td>
</tr>
<tr>
<td>Decrease in vLAP ≤ 5 mmHg</td>
<td>1.51 (0.55-4.12)</td>
<td>0.42</td>
</tr>
<tr>
<td>STS-PROM for repair</td>
<td>1.1 (1.03-1.18)</td>
<td>0.008</td>
</tr>
<tr>
<td>DMR</td>
<td>0.69 (0.23-2.04)</td>
<td>0.5</td>
</tr>
<tr>
<td>Multivariable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>mLAP ≥ 15 mmHg</td>
<td>2.85 (0.89-7.94)</td>
<td>0.081</td>
</tr>
<tr>
<td>vLAP ≥ 25 mmHg</td>
<td>0.6 (0.24-1.49)</td>
<td>0.27</td>
</tr>
<tr>
<td>Decrease in vLAP ≤ 5 mmHg</td>
<td>1.40 (0.51-3.82)</td>
<td>0.51</td>
</tr>
<tr>
<td>STS-PROM for repair</td>
<td>1.09 (1.01-1.18)</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>1.11 (1.04-1.20)</td>
<td>0.004</td>
</tr>
<tr>
<td></td>
<td>1.10 (1.02-1.19)</td>
<td>0.011</td>
</tr>
</tbody>
</table>
Conclusion

- The impact of LAP assessment in determining clinical improvement of patients after MitraClip is modest, and not incrementally better than residual MR severity alone.

- Our findings suggested the need for comprehensive hemodynamic assessments when evaluating the results of MitraClip procedure and their impact on long-term outcomes.

Thank you for your attention!!

First Trial to evaluate an injectable biomaterial delivered via percutaneous transendocardial cardiac injections.
Myocardial Infarction

- Myocardial infarction
- Death of cardiomyocytes
- ECM Degradation
- Scar tissue (fibrosis)
- Left ventricular remodeling
- Heart Failure

Why Your Cardiac Myocytes and Stem Cells Need an Extracellular Matrix (ECM)

- Consists of families of fibrous proteins including: collagen, fibronectin, laminen, proteoglycans.
- ECM degraded following STEMI (MMPs, etc)
- Adhesion to ECM necessary for progenitor cell differentiation, growth and tissue regeneration.
- Prevents apoptotic loss - Anoikis
- Provides a reservoir of growth factors (VEGF, b-FGF, TGF-β).
Using Biomaterials as a Surrogate of the Extracellular Matrix (ECM)

- Synthetic and Natural Materials.
  - Alginate – PRESERVATION-AMI Trial (IK-5001)
    - Lone Star Heart, Inc.
  - Collagen and fibrin-based matrices
  - Self-assembling nano-peptides
  - Small Intestinal Submucosa (SIS)-Cook Biotech, Inc.
  - Porcine Cardiac ECM – Ventryx, Inc.

Intracoronary Alginate to Infarct Zone

Leor et al. JACC 2009
Bioabsorbable Intracoronary Matrix for Prevention of Ventricular Remodeling After Myocardial Infarction

- 303 patients with large STEMI and LV dysfunction randomized 2:1 to Alginate ECM vs. Saline 2-5 days following STEMI.
- No change in LVEDVI at 6 months (ECM=14.1±29 ml/m2 vs. 11.7 ± 27 ml/m2).
- MVO may have prevented uptake of alginate in infarct zone.

J Amer Coll Cardiol 2016

Rationale for Using a Porcine-Derived Cardiac Extracellular Matrix

- Cellular and Tissue response to ECM more important than physical support of infarct region to prevent adverse LV remodeling.
- Open, porous scaffold allows cells and blood vessels to permeate hydrogel with ECM cues of normal myocardium.
- Ventrigel has appropriate viscosity and gelation kinetics to facilitate transendocardial delivery.
- Available as an off-the-shelf product, more economical than cell therapy.
Decellularized Porcine Cardiac Matrix Hydrogel


RESEARCH ARTICLE

TISSUE ENGINEERING

Safety and Efficacy of an Injectable Extracellular Matrix Hydrogel for Treating Myocardial Infarction


- Cardiac-derived porcine ECM delivered by intramyocardial injections (NOGA) to Yucatan swine (45 kg) heart 2 weeks following myocardial infarction (coiling).
- At 3 months Follow-up:
  - ECM pigs had smaller increase in infarct size (NOGA measurement)
    (Control = 11 cm²; ECM = 2.1 cm²), improved LVEF and smaller volumes.
  - Increased endocardial muscle layer with neovascularization.
  - No significant arrhythmias in ECM group.
  - Reduced fibrosis
  - ECM resorbed by 28 days
Fig. 1 Echocardiographic data show improvement after injection of myocardial matrix.


Histological characterization of infarcted pig hearts.

A = ECM heart
B = Non-injected Control
C = saline injected Control
D = troponin staining
E = % muscle in infarct Area
F = fibrosis
G = ECM – neovasc.
H = Control – no neovasc.

Phase 1, First-in-Man Clinical Trial

- 15 patients (12 Male) with history of first STEMI (2 months < STEMI < 3 years) treated with PCI.

- LV dysfunction (25% < LVEF < 45%).

- Electromechanical mapping with NOGA catheter.

- Intramyocardial injections of Ventrigel (Myostar Catheter) 18 injections x 0.3 ml

- Cardiac MRI (LVEF / Volumes), 6-min Walk, KCCQ, NYHA (baseline, 3, 6 months)

**TABLE 1 Patient Demographics and Baseline Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>Ventrigel Treatment (N = 10)</th>
<th>Patients &lt;32 Months Post-MI at Treatment (n = 7)</th>
<th>Patients &gt;32 Months Post-MI at Treatment (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, yrs</strong></td>
<td>59.6 ± 8.8</td>
<td>57.7 ± 10.3</td>
<td>61.3 ± 7.5</td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td>5 (20.0)</td>
<td>2 (28.6)</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td><strong>White, non-Hispanic</strong></td>
<td>12 (82.0)</td>
<td>6 (85.7)</td>
<td>6 (75.0)</td>
</tr>
<tr>
<td><strong>White, Hispanic</strong></td>
<td>1 (6.7)</td>
<td>1 (14.3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td><strong>African American</strong></td>
<td>2 (13.3)</td>
<td>0 (0)</td>
<td>2 (28.6)</td>
</tr>
<tr>
<td><strong>Body mass index, kg/m²</strong></td>
<td>30.0 (4.4)</td>
<td>29.1 (4.1)</td>
<td>30.7 (4.7)</td>
</tr>
<tr>
<td>Tobacco use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Former</td>
<td>10 (66.7)</td>
<td>5 (71.4)</td>
<td>5 (62.5)</td>
</tr>
<tr>
<td>Current</td>
<td>1 (6.7)</td>
<td>1 (14.3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>3 (20.0)</td>
<td>2 (28.6)</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>7 (46.7)</td>
<td>4 (57.1)</td>
<td>3 (37.5)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>12 (80.0)</td>
<td>4 (57.1)</td>
<td>8 (100)</td>
</tr>
<tr>
<td>Previous PCI</td>
<td>15 (100)</td>
<td>7 (100)</td>
<td>8 (100)</td>
</tr>
<tr>
<td>Previous CARG</td>
<td>3 (20.0)</td>
<td>0 (0)</td>
<td>3 (37.5)</td>
</tr>
<tr>
<td>NYHA functional class</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>3 (20.0)</td>
<td>1 (14.3)</td>
<td>2 (25.0)</td>
</tr>
<tr>
<td>II</td>
<td>11 (73.3)</td>
<td>5 (71.4)</td>
<td>6 (75.0)</td>
</tr>
<tr>
<td>III</td>
<td>1 (6.7)</td>
<td>1 (14.3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Time from MI to injection (months)</td>
<td>15.2 ± 10.6</td>
<td>6.5 ± 2.9</td>
<td>22.8 ± 8.7</td>
</tr>
</tbody>
</table>

Values are mean ± SD or n(%).  
CARG = coronary artery bypass grafting, MI = myocardial infarction, NYHA = New York Heart Association,  
PCC = percutaneous coronary intervention.
Phase 1 Results

15 patients treated with VentriGel

Primary Endpoint: Safety:
VentriGel was well-tolerated

Secondary Endpoints:
Encouraging efficacy signals
- Statistically significant improvements in 6 min walk test
- Symptoms score trending toward improvement

Traverse et al., JACC: BTS, 2019

Phase 1 Results – Stratified by Infarct Age

80% maintained/improved ESV or EDV at 6 months
Late MI patients (>12 mo post-MI) identified as major responders (n=8)

Traverse et al., JACC: BTS, 2019
CONCLUSIONS

- Ventrigel was delivered safely by intramyocardial injections to post-MI patients with LV dysfunction.
- No significant adverse events through 1-year of follow-up.
- Subjects with older infarcts (> 12 months) appeared to have improved LV remodeling compared to recent infarcts.
- These results form the basis of a larger Phase 2 clinical trial.

Temporal Changes of Noninvasive Electrocardiographic Risk Factors for Sudden Cardiac Death in Post-Myocardial Infarction Patients with Preserved Ejection Fraction: Insights from the PRESERVE-EF

Iosif Xenogiannis, MD

Minneapolis Heart Institute, Abbott Northwestern Hospital
Minneapolis Heart Institute Foundation
Disclosure Statement of Financial Interest

I, Iosif Xenogiannis DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

Sudden Cardiac Death-The Burden

- Accounts for approximately 20% of total mortality in industrialized countries.

- The incidence of SCD in the US is around 400,000 / year.

- Around 50% of men and 2/3 of women die suddenly without previously having CAD symptoms.
Sudden Cardiac Death-Risk Stratification

- Risk stratification methods remain suboptimal, ignoring the majority of patients who are at risk.

### Table 1

<table>
<thead>
<tr>
<th>% of all SCD</th>
<th>Predictability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not diagnosed with heart disease</td>
<td>45</td>
</tr>
<tr>
<td>History of heart disease: LVEF &lt; 40%</td>
<td>40</td>
</tr>
<tr>
<td>History of heart disease: LVEF ≥ 40%</td>
<td>13</td>
</tr>
<tr>
<td>Genetically based arrhythmic disease</td>
<td>2</td>
</tr>
</tbody>
</table>

(SCD, sudden cardiac death; LVEF, left ventricular ejection fraction.)


Circulation. 2018;138:e272–e391

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**THE PRESERVE-EF STUDY**

### Arrhythmic risk stratification in post-myocardial infarction patients with preserved ejection fraction: the PRESERVE EF study

- Post-MI patients with LVEF≥40%
- With no further evidence of ischemia or no targets for revascularization
- (40 days post-PCI / 90 after CABG)

Konstantinos A. Gatzoulis 1, Dimitrios Tsiaakis 1, Petros Arsenos 1, Christos-Konstantinos Antoniou 1, Polychronis Dilaveris 1, Svevos Sideris 2, Emmanouel Kanopakis 1, Emmanouil Simantarakis 1, Panagiotis Korantzopoulos 1, Ioannis Goudevenos 1, Panagiota Flevani 1, Estathios Iliodromitis 1, Antonios Sideris 1, Vassilios Vasiliou 1, Nikolaos Fragakis 1, Konstantinos Trachanas 1, Michail Vernardos 1, Ioannis Konstantinou 1, Konstantinos Tsimos 1, Iosif Xenogiannis 1, Konstantinos Vlachos 1, Athanasios Saplaouras 1, Konstantinos Triantafyllou 1, Ioannis Kallikazaros 1, and Dimitrios Toutouzis 1

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Two-step approach

First Step

1. LPs (2/3) on SAECG (45 min Holter)
2. >30 PVCs/hour on 24-hour ECG monitoring
3. ≥ 1 nsVT episode on 24-hour ECG monitoring
4. QTc (Fridericia) ≥ 440 msec (men) or QTc ≥ 450 msec (women)
5. SDNN < 75 msec on 24-hour ECG monitoring
6. TWA ≥ 65 μV (2 channels) on 24-hour ECG monitoring
7. Abnormal heart rate turbulence (post-PVC - onset ≥ 0% AND slope ≤ 2.5 msec/rri) AND deceleration capacity (≤ 4.5 msec)

Second Step

If VT (both monomorphic and polymorphic) or VF induced ICD implantation
If any of the previous was positive

Table 3  Characteristics of patients with appropriate ICD activation

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Age</th>
<th>Gender</th>
<th>Infarction type</th>
<th>Culprit vessel</th>
<th>NYHA class</th>
<th>LVEF</th>
<th>LVEDD mm</th>
<th>β-blocker dose (metoprolol equivalents)</th>
<th>NIRFs present</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>64</td>
<td>Male</td>
<td>STEMI</td>
<td>LCx</td>
<td>1</td>
<td>45</td>
<td>57</td>
<td>75</td>
<td>LPs</td>
</tr>
<tr>
<td>2</td>
<td>67</td>
<td>Male</td>
<td>STEMI</td>
<td>LCx</td>
<td>1</td>
<td>47</td>
<td>46</td>
<td>125</td>
<td>LPs, PVCs, nsVT</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>T</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>T</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>T</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>59</td>
<td>Male</td>
<td>STEMI</td>
<td>LAD/RCA</td>
<td>1</td>
<td>50</td>
<td>60</td>
<td>75</td>
<td>LPs, QTC, nsVT</td>
</tr>
<tr>
<td>7</td>
<td>70</td>
<td>Male</td>
<td>STEMI</td>
<td>3 vessels</td>
<td>1</td>
<td>40</td>
<td>55</td>
<td>100</td>
<td>LPs, QTC, TWA</td>
</tr>
<tr>
<td>8</td>
<td>72</td>
<td>Male</td>
<td>STEMI</td>
<td>LCx</td>
<td>1</td>
<td>50</td>
<td>52</td>
<td>200</td>
<td>nsVT</td>
</tr>
<tr>
<td>9</td>
<td>64</td>
<td>Male</td>
<td>STEMI</td>
<td>3 vessels</td>
<td>2</td>
<td>50</td>
<td>56</td>
<td>65</td>
<td>QTc</td>
</tr>
<tr>
<td>Average</td>
<td>63</td>
<td></td>
<td></td>
<td></td>
<td>1.1</td>
<td>47</td>
<td>52.8</td>
<td>107</td>
<td></td>
</tr>
</tbody>
</table>
NIRFs Temporal Changes

- NIRFs of 80 patients from one center participating in the Preserve-EF were evaluated 49 (IQR 44, 65) days post-MI and then re-evaluated 361 (347, 378) days after.

<table>
<thead>
<tr>
<th>Basic characteristics</th>
<th>N=80</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)(^1)</td>
<td>56±10</td>
</tr>
<tr>
<td>Male gender (%)</td>
<td>88 (70)</td>
</tr>
<tr>
<td>BMI (kg/m²)(^1)</td>
<td>27±4</td>
</tr>
<tr>
<td>Smoking (current) (%)</td>
<td>75 (60)</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>23 (18)</td>
</tr>
<tr>
<td>Dyslipidemia (%)</td>
<td>71 (57)</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>44 (35)</td>
</tr>
<tr>
<td>STEMI (%)</td>
<td>61 (49)</td>
</tr>
<tr>
<td>One-vessel disease (%)</td>
<td>65 (81)</td>
</tr>
<tr>
<td>Culprit vessel (%)</td>
<td></td>
</tr>
<tr>
<td>LAD (%)</td>
<td>39 (29)</td>
</tr>
<tr>
<td>RCA (%)</td>
<td>39 (29)</td>
</tr>
<tr>
<td>LCX (%)</td>
<td>21 (21)</td>
</tr>
<tr>
<td>Ramus (%)</td>
<td>1.3 (1)</td>
</tr>
<tr>
<td>NYHA I (%)</td>
<td>90 (72)</td>
</tr>
<tr>
<td>Hb g/dl(^1)</td>
<td>14.1±1.1</td>
</tr>
<tr>
<td>Glu mmol/L(^2)</td>
<td>5.88 (5.16, 7.77)</td>
</tr>
<tr>
<td>Cr μmol/L(^2)</td>
<td>70.7 (61.9, 88.4)</td>
</tr>
<tr>
<td>K meq/L(^2)</td>
<td>4.3 (4.1, 4.6)</td>
</tr>
<tr>
<td>LDL mmol/L(^2)</td>
<td>3.2 (2.4, 3.8)</td>
</tr>
<tr>
<td>HDL mmol/L(^2)</td>
<td>0.96 (0.83, 1.1)</td>
</tr>
<tr>
<td>TG mmol/L(^2)</td>
<td>1.3 (1.0, 1.7)</td>
</tr>
<tr>
<td>B-blockers (%)</td>
<td>94 (75)</td>
</tr>
<tr>
<td>ACE inhibitors/ARB (%)</td>
<td>88 (70)</td>
</tr>
<tr>
<td>Statin (%)</td>
<td>99 (79)</td>
</tr>
<tr>
<td>Aspirin (%)</td>
<td>100 (80)</td>
</tr>
<tr>
<td>P2Y12 inhibitors (%)</td>
<td>100 (80)</td>
</tr>
</tbody>
</table>

\(^1\) Mean ± standard deviation  
\(^2\) Median (interquartile range)
<table>
<thead>
<tr>
<th>Echocardiographic measurements/ HR, basic electrocardiographic intervals</th>
<th>First assessment</th>
<th>Second assessment</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF(%)(^1)</td>
<td>50±5</td>
<td>52±6</td>
<td>0.1690</td>
</tr>
<tr>
<td>LVEDD mm(^1)</td>
<td>48±5</td>
<td>48±4</td>
<td>0.8723</td>
</tr>
<tr>
<td>HR bpm(^1)</td>
<td>68±8</td>
<td>70±9</td>
<td>0.1650</td>
</tr>
<tr>
<td>QRS msec(^2)</td>
<td>88 (80, 100)</td>
<td>89 (80, 100)</td>
<td>0.4848</td>
</tr>
<tr>
<td>P msec(^2)</td>
<td>100 (80, 116)</td>
<td>108 (87, 120)</td>
<td>0.0772</td>
</tr>
<tr>
<td>PR msec(^2)</td>
<td>160 (140, 180)</td>
<td>159 (140, 170)</td>
<td>0.8707</td>
</tr>
<tr>
<td>QT msec(^2)</td>
<td>413 (400, 440)</td>
<td>402 (400, 420)</td>
<td>0.1934</td>
</tr>
<tr>
<td>RR msec(^2)</td>
<td>1001±131</td>
<td>966±135</td>
<td>0.0951</td>
</tr>
</tbody>
</table>

\(^1\) Mean ± standard deviation
\(^2\) Median (interquartile range)

No difference in the incidence of NIRFs between the two evaluations

**Incidence of NIRFs during the first vs second Holter assessment**

- Positive LPs (≥ 2/3)
- PVCs > 30/h
- Presence of NSVT
- SDNN ≤ 75 ms
- QTc > 440 ms (men), > 450 ms (women)
- DC ≤ 4.5 ms and HRT onset ≥ 20% and HRT slope ≤ 2.5 ms
- T-wave alternans ≥ 65 μV in two holter channels

<table>
<thead>
<tr>
<th>Condition</th>
<th>First Assessment</th>
<th>Second Assessment</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive LPs (≥ 2/3)</td>
<td>28%</td>
<td>29%</td>
<td>0.860</td>
</tr>
<tr>
<td>Presence of NSVT</td>
<td>9%</td>
<td>11%</td>
<td>0.598</td>
</tr>
<tr>
<td>SDNN ≤ 75 ms</td>
<td>9%</td>
<td>9%</td>
<td>0.349</td>
</tr>
<tr>
<td>QTc &gt; 440 ms (men), &gt; 450 ms (women)</td>
<td>4%</td>
<td>4%</td>
<td>1.000</td>
</tr>
<tr>
<td>DC ≤ 4.5 ms and HRT onset ≥ 20% and HRT slope ≤ 2.5 ms</td>
<td>18%</td>
<td>18%</td>
<td>1.000</td>
</tr>
<tr>
<td>T-wave alternans ≥ 65 μV in two holter channels</td>
<td>3%</td>
<td>4%</td>
<td>1.000</td>
</tr>
</tbody>
</table>

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No difference in the absolute values of NIRFs between the two evaluations

<table>
<thead>
<tr>
<th>Non-invasive risk factors</th>
<th>First assessment</th>
<th>Second assessment</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LPS1</td>
<td>97 (89, 104)</td>
<td>99 (90, 108)</td>
<td>0.4223</td>
</tr>
<tr>
<td>TQRS msec1</td>
<td>32 (24, 39)</td>
<td>34 (26, 40)</td>
<td>0.3296</td>
</tr>
<tr>
<td>LAS msec1</td>
<td>36 (17, 69)</td>
<td>28 (15, 69)</td>
<td>0.3936</td>
</tr>
<tr>
<td>LPS positive (%)</td>
<td>27.5</td>
<td>28.8</td>
<td>0.8604</td>
</tr>
<tr>
<td>PVCs1</td>
<td>12 (2, 139)</td>
<td>19 (2, 343)</td>
<td>0.5227</td>
</tr>
<tr>
<td>&gt; 30 PVCs/ hr (%)</td>
<td>8.8</td>
<td>11.3</td>
<td>0.5982</td>
</tr>
<tr>
<td>NSVT (%)</td>
<td>8.8</td>
<td>5</td>
<td>0.3486</td>
</tr>
<tr>
<td>SDNN msec1</td>
<td>127 (108, 148)</td>
<td>128 (112, 154)</td>
<td>0.7548</td>
</tr>
<tr>
<td>Abnormal SDNN (%)</td>
<td>3.8</td>
<td>3.8</td>
<td>1.0000</td>
</tr>
<tr>
<td>QTc msec2</td>
<td>425±19</td>
<td>426±16</td>
<td>0.8853</td>
</tr>
<tr>
<td>QTc &gt; 440 msec men, &gt; 450 msec women (%)</td>
<td>17.5</td>
<td>17.5</td>
<td>1.0000</td>
</tr>
<tr>
<td>TO (%)1</td>
<td>-0.02 (-0.04, -0.01)</td>
<td>-0.02 (-0.04, -0.01)</td>
<td>0.6720</td>
</tr>
<tr>
<td>TS ms/mi1</td>
<td>9.7 (5.5, 14.9)</td>
<td>8.8 (4.6, 17.4)</td>
<td>0.8631</td>
</tr>
<tr>
<td>Dm msec1</td>
<td>6.7 (4.75, 8.8)</td>
<td>6.9 (5.1, 8.1)</td>
<td>0.8417</td>
</tr>
<tr>
<td>Abnormal HR turbulence / DC (%)</td>
<td>2.5</td>
<td>3.8</td>
<td>1.0000</td>
</tr>
<tr>
<td>T-wave alternans ≥65 µV (%)</td>
<td>6.25</td>
<td>6.25</td>
<td>1.0000</td>
</tr>
</tbody>
</table>

1 Mean ± standard deviation
2 Median (interquartile range)

Mean EF= 50% ± 5%

*Incidence of positive NIRFs 49 (44, 65) days post MI was 55%*

Mean EF= 52% ± 6%

*Incidence of positive NIRFs 361 (347, 378) days post MI was 54%*
But...

- Five patients (6.3%) without any NIRFs during the first assessment had at least one positive NIRF at the second assessment.

- Six patients (7.5%) with at least one NIRF at baseline had no positive NIRFs at one year.

Limitations

Due to the small number of patients, this substudy might be lacking sufficient statistical power to detect differences in less frequent NIRFs, such as SDNN (2.8%), and heart rate turbulence/deceleration capacity (2.8%).
Conclusions

While the prevalence of the examined electrocardiographic NIRFs between the two examinations was similar on a population basis, some patients without NIRFs at baseline developed NIRFs at one year and vice versa, highlighting the need for risk factor reassessment during follow-up.