Use of the Wearable Cardioverter Defibrillator in Cardiac Patients at High Risk of Sudden Arrhythmic Death

Heart Failure 2017 – An Update on Therapy
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Heart Failure in the U.S.

- Nearly 6 million HF patients in the U.S. and ~1 million hospitalizations with HF as primary diagnosis.
- By 2030 prevalence expected to be 8 million.
- Over 300,000 deaths a year and mortality rates that remain at 50% at 5 years from diagnosis.
- Nearly one in four patients hospitalized with HF is re-hospitalized within 30 days of discharge.
- The 30 day risk-standardized re-hospitalization rates in HF have risen from 17.3% in 1993 to 24.1% in 2014.
- Between 12 to 15 million outpatient office visits.
- Direct costs of over 30 billion dollars a year (that will rise to 70 billion in 2030 (~80% due to hospitalizations).
HF Is Deadlier Than HIV and Some Cancers

- The average life expectancy of Americans with HIV is 22.5 years\(^1\)

**5-year Death Rates of Common Cancers**

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Rate, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast Cancer</td>
<td>11(^2)</td>
</tr>
<tr>
<td>Hodgkin's Lymphoma</td>
<td>15(^2)</td>
</tr>
<tr>
<td>Non-Hodgkin's</td>
<td>31(^2)</td>
</tr>
<tr>
<td>Colon and Rectum</td>
<td>35(^2)</td>
</tr>
<tr>
<td>Leukemia</td>
<td>43(^2)</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>48(^3)</td>
</tr>
</tbody>
</table>

HIV, human immunodeficiency virus

**References:**
Chronic HF Patients Have Increased Risk With Higher NYHA Class\textsuperscript{1,2}

Mean follow-up=1y
Cause of death

<table>
<thead>
<tr>
<th></th>
<th>Other</th>
<th>HF</th>
<th>Sudden cardiac death</th>
</tr>
</thead>
<tbody>
<tr>
<td>NYHA Class II</td>
<td>6.3</td>
<td>1.5</td>
<td>0.8</td>
</tr>
<tr>
<td>n = 1636</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Slight limitation of physical activity, comfortable at rest but ordinary physical activity results in symptoms of HF\textsuperscript{2}</td>
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</table>

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<th></th>
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<th>HF</th>
<th>Sudden cardiac death</th>
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</thead>
<tbody>
<tr>
<td>NYHA Class III</td>
<td>10.5</td>
<td>1.7</td>
<td>2.7</td>
</tr>
<tr>
<td>n = 2210</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marked limitation of physical activity, comfortable at rest but less than ordinary activity causes symptoms of HF\textsuperscript{2}</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
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<th>HF</th>
<th>Sudden cardiac death</th>
</tr>
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<tbody>
<tr>
<td>NYHA Class IV</td>
<td>18.6</td>
<td>2.0</td>
<td>10.4</td>
</tr>
<tr>
<td>n = 145</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest\textsuperscript{2}</td>
<td></td>
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</tr>
</tbody>
</table>

NYHA, New York Heart Association functional classifications (not including class I).

**References:**
Mode of Death by NYHA Class

NYHA II
- HF: 12%
- SD: 64%
- Other: 24%

NYHA III
- HF: 26%
- SD: 59%
- Other: 15%

NYHA IV
- HF: 56%
- SD: 33%
- Other: 11%
Targeting RAS and SNS Activation is Guideline Recommended

Improvement in EF with Beta Blockers Occurs Over Time

- A HF patient’s cardiac function can improve from the benefits of optimized medical therapy
  - IMAC-2 study showed a mean LVEF increase of 17% in newly diagnosed cardiomyopathy patients\(^1\)
  - REFINE Study average relative improvement in EF was 18% at 8-10 weeks\(^2\)

\(^1\) McNamara D et al.. Clinical and Demographic Predictors of Outcomes in Recent Onset Dilated Cardiomyopathy. JACC 2011;58:1112-8.
\(^3\) Hall S, et al. Time Course of Improvement in Left Ventricular Function, Mass and Geometry in Patients with Congestive Heart Failure Treated With Beta-Adrenergic Blockade. JACC 1995;25:1154-61
Beta Blocker Effects in Clinical Trials

- Beta blocker doses effective in HF are generally achieved in 8 to 12 weeks and do not impart any mortality benefit until at least 3 months

Risk of SCD Post-MI is Highest Over the First 30 Days

- Post-MI patients with heart failure are at 4-6 times greater risk of SCD in the first 30 days after MI
- 83% of SCA occurred after hospital discharge.
- 74% of those resuscitated in the first 30 days were alive at 1 year

Solomon SD, et al. Sudden Death in Patients with Myocardial Infarction and Left Ventricular Dysfunction, Heart Failure, or Both. NEJM 2005; 352: 2581-2588.
ICD Therapy: The “Gold Standard” for SCD Protection

SCD-HeFT Mortality

n = 2521
Absolute Mortality Risk Reduction at 5 years: 7.2%
Absolute Mortality Risk Reduction at 12 years: 5%

Guidelines Recommend Waiting Before ICD Implantation To Give the Myocardium Time To Heal

Ejection Fraction
≤ 35%

Post-MI

With Revascularization (PCI or CAB)
ICD waiting period > 3 mo

Initiate or Titrate Medical Therapy
Beta Blocker – ACE/ARB – Aldosterone Antagonist

Discharge home; Continue optimization of medical therapy
Consider consultation with heart rhythm specialist / consider wearable cardioverter defibrillator

Reassess EF at 3 mo
Reassess EF at 40 d

EF ≤ 35%

Without Revascularization
ICD waiting period > 40 d

Refer for consultation with heart rhythm specialist
Identifying the Opportunity
Schematic Depiction of Comprehensive HF Care

Allen et al., Decision Making in Advanced Heart Failure: A Scientific Statement From the American Heart Association Circulation 2012, 125:1928-1952
FDA Indications for WCD Use

- The LifeVest Wearable Cardioverter Defibrillator (WCD) System is indicated for adult patients who are at risk for sudden cardiac arrest and are not candidates for or who refuse an implantable defibrillator.

- WCD Offers Protection From SCD Time To Recovery and Assess Long-Term Risk
  - Protection from SCA during medical therapy optimization.
  - Allows physician to assess long-term arrhythmic risk at the end of the Medicare ICD waiting period (40 days post-MI and 90 days post-PTCA/post-CABG).
LifeVest Features

ECG Electrodes
- Dry & non-adhesive
- 4 electrodes providing 2 channels of monitoring

Self-Gelling Defibrillation Electrodes

Response Buttons

Monitor
- 150 joules biphasic
- Stores ECG, daily use, etc.
Alarm Sequence

1. Arrhythmia detected, activating vibration alert (continues throughout sequence).
2. Siren alerts begin (continues throughout sequence).
3. Siren alerts get louder.
5. Gel release.
7. Treatment shock.
Example Event ECG

24 seconds between top and bottom

onset

shock

recovery
LifeVest WCD by the Numbers

- 98% first shock success rate
- 92% shocked event survival (conscious ER arrival or stayed at home)
- Most (73%) treated within 60 seconds (remaining delayed from response button use or VT programming)
- Average duration of use is 2 to 3 months
- Median daily use is 94% (22.6 hours/day)
Purpose:
• To provide prospective data on the safety and efficacy of a bridging strategy with the WCD in a real world setting

Design:
• WCD (LifeVest) prescription in the US
• Informed consent for study participation
• Acquisition of baseline clinical data
• Wearing time: 3 months
• Clinical and arrhythmic event acquisition
• WCD return: end of use evaluation
WEARIT-II Registry: Results From The Prospective Registry Of Patients Using WCD

- N= 2,000 patients enrolled in the US
  - Currently enrolling patients in Europe, Israel
- Data collection: August 2011 – February 2014
- Data management: University of Rochester

ICM
- 805 pts (40.3%)

NICM
- 927 pts (46.4%)

Cong/Inherited
- 268 pts (13.4%)

Kutyifa, et al. Use of the Wearable Cardioverter Defibrillator in High-Risk Cardiac Patients: Data from the Prospective Registry of Patients Using the Wearable Cardioverter Defibrillator (WEARIT-II Registry). Circulation 2015; DOI: 10.1161/CIRCULATIONAHA.115.015677 [epub ahead of print].
Probability of VT/VF at 3 months for WEARIT-II patients was nearly double that of MADIT-RIT groups B and C
## WEARIT-II: Safety End Points

<table>
<thead>
<tr>
<th>TYPE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=2000</td>
</tr>
<tr>
<td>Inappropriate Rx, n (%)</td>
<td>10 (0.5%)</td>
</tr>
<tr>
<td>Death, n (%) with the WCD</td>
<td>3 (0.2%)*</td>
</tr>
</tbody>
</table>

* WCD detected asystole at the time of death in all 3 patients

No death related to unsuccessful termination of VT/VF
Outcomes Following LifeVest Use
WEARIT-II Registry

- Prospective registry of WCD patients
- Results in patients representative of the HF population
  - 41%: LVEF improved and patients did not need an ICD
  - 42%: LVEF did not improve >35% and patients received an ICD

Kutyifa, V et al., Results From The Prospective Registry Of Patients Using The Wearable Defibrillator (WEARIT-II Registry), presented as Late Breaking Clinical Trial at European Society of Cardiology, August 30, 2014. Available at http://congress365.escardio.org/Presentation/106368#.VES87vmsUmk
WEARIT-II

ICD Implantation Rate by Disease Etiology

Patients, %

- **Ischemic CMP**: 53% Received ICD, 49% EF improved
- **Nonischemic CMP**: 46% Received ICD, 54% EF improved
- **Congenital/Inherited**: 59% Received ICD, 41% EF improved

Kutyifa V, et al. ESC. 2014.[7]
ECG Review

ECG information captured by the LifeVest can be used to diagnose:

- Sustained VT/VF
- Non-sustained VT
- Atrial arrhythmias/SVT
- Severe bradycardia/Asystole
WEARIT-II
Arrhythmic Events

1 in 14 patients diagnosed with an arrhythmia requiring intervention while wearing the LifeVest

<table>
<thead>
<tr>
<th>Event Description</th>
<th>Patients (%)</th>
<th>Events (events/pt)</th>
<th>Event Rate Per 100 Pt-Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Sustained VT/VF *</td>
<td>41 (2.1%)</td>
<td>120 (2.9)</td>
<td>22</td>
</tr>
<tr>
<td>WCD Therapy for VT/VF</td>
<td>22 (1.1%)</td>
<td>30 (1.36)</td>
<td>5</td>
</tr>
<tr>
<td>Non-sustained VT</td>
<td>28 (1.4%)</td>
<td>164 (5.9)</td>
<td>30</td>
</tr>
<tr>
<td>Atrial arrhythmias/SVT</td>
<td>72 (3.6%)</td>
<td>561 (7.8)</td>
<td>121</td>
</tr>
<tr>
<td>Asystole</td>
<td>6 (0.3%)</td>
<td>9 (1.5)</td>
<td>2</td>
</tr>
</tbody>
</table>

7.4% or 1/14

- Treated VT/VF and sustained VT that spontaneously terminated during use of the response button or during the extended detection time
- Median Wear Time = 90 days
WCD Recording From a Patient with Unexplained Syncope
WCD Recording Reveals Atrial Fibrillation

Patient Baseline

Patient ECG downloaded and viewed on LifeVest Network
The Potential of Remote Data Management to Impact Patient Care

- Based on the WEARIT II registry results, if your next 100 patients were prescribed the WCD:
  
  2 patients will experience a sustained VT/VF event – 1 of which will require a treatment and the other will self-terminate and the patient will likely be a candidate for an ICD.

  1 patient will have non-sustained VT, is likely a candidate for an EP study, and, if inducible, is a candidate for an ICD.

  4 patients will experience supraventricular arrhythmias which will likely lead to more evaluation. In the majority of cases, those will likely require ablation.

  1 patient may survive asystole or severe bradycardia and will likely require pacing therapy.
WEARIT-II: Summary

- In a real world setting, a management strategy that incorporates the WCD can be safely used to bridge a decision for appropriate ICD therapy in patients with acquired, inherited, and congenital, heart disease:
  - Very low rate of inappropriate therapies
  - Safe, no death related to WCD
  - 1 in 2 patients will improve and thus avoid ICD implantation while being protected in a high risk period
- Potentially treatable rhythm disturbances were noted in 1/14 patients.
Guidelines and Recommendations: LifeVest

- **2015 ESC Guidelines for Management of Patients with Ventricular Arrhythmias and Prevention of Sudden Cardiac Death**
  - LifeVest is a Class II recommendation for patients with poor systolic function until they are candidates for ICD therapy.

- **2006 International Society for Heart and Lung Transplantation Guidelines for the Care of Cardiac Transplant Candidates**
  - LifeVest is a Class I recommendation

  - LifeVest is an alternative to early re-implantation when there is concern for ongoing infection

- **2014 HRS/ACC/AHA Expert Consensus Statement on the Use of Implantable Cardioverter-Defibrillator Therapy in Patients Who Are Not Included or Not Well Represented in Clinical Trials**
  - LifeVest may play a role in patients at risk of sudden cardiac death in the early period after revascularization or awaiting cardiac transplantation

- **2014 AHA/ACC Guidelines for the Management of Patients with Non-ST-Elevation Acute Coronary Syndromes**
  - LifeVest may be considered for patients with ACS and reduced LVEF, when an ICD is not indicated

- **2014 EHRA/HRS/APHRS Expert Consensus on Ventricular Arrhythmias**
  - LifeVest recommended for high risk patients with ACS during medical therapy optimization.

- WCDs can serve as temporary means of preventing arrhythmic death without the need for bystander response to cardiac arrest.
- WCD use may be appropriate in clinical circumstances associated with transient increased arrhythmic risk.
<table>
<thead>
<tr>
<th>Indication</th>
<th>Class</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of WCDs is reasonable when there is a clear indication for an implanted/</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>permanent device accompanied by a transient contraindication or interruption in ICD care such as infection.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of WCDs is reasonable as a bridge to more definitive therapy such as cardiac transplantation.</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Use of WCDs may be reasonable when there is concern about a heightened risk of SCD that may resolve over time or with treatment of left ventricular dysfunction; for example, in ischemic heart disease with recent revascularization, newly diagnosed non-ischemic dilated cardiomyopathy in patients starting guideline-directed medical therapy, or secondary cardiomyopathy (tachycardia mediated, thyroid mediated, etc.) in which the underlying cause is potentially treatable</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>WCDs may be appropriate as bridging therapy in situations associated with increased risk of death in which ICDs have been shown to reduce SCD but not overall survival such as within 40 days of MI.</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>WCDs should not be used when non-arrhythmic risk is expected to significantly exceed arrhythmic risk, particularly in patients who are not expected to survive &gt;6 mo.</td>
<td>III: No benefit</td>
<td>C</td>
</tr>
</tbody>
</table>
Conclusions

• Heart failure is a common and often lethal condition.
• OMT optimization takes time and is different for every patient.
• Patients are at risk of SCD as medical therapy is initiated.
• Post-MI patients with heart failure are at 4-6 times greater risk of SCD in the first 30 days after MI.
• The WCD is an effective tool to protect HF patients with low EF during medication titration while long-term risk is being determined.
• In the WEARIT II Registry, 1 in 14 patients were diagnosed with an arrhythmia requiring intervention with a WCD.
• In addition to protection from SCD, the WCD captures information about other arrhythmias that require treatment.