Prevention of sudden cardiac death:  
With an emphasis on sudden cardiac death from ventricular arrhythmias

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Faculty/Presenter Disclosure

• Faculty: Andrew C. T. Ha, MD

• Relationship(s) with commercial interests:
  – Advisory board: Bayer Inc.
Objectives

1) Overview of the incidence and pathophysiology of sudden cardiac death (SCD) in the post-myocardial infarction (MI) population, with a particular emphasis on SCD related to ventricular arrhythmias (VF/VT).

2) Review of the role of implantable cardioverter defibrillators (ICD) in the management of sudden cardiac death amongst patients with ischemic heart disease.

3) Discuss areas of uncertainty/controversy in the use of ICD’s for SCD management amongst post-MI patients.
Sudden cardiac death: Definition

*Sudden cardiac death* is natural death due to cardiac causes, heralded by abrupt loss of consciousness within *one hour* of the onset of acute symptoms, as in an individual with or without known pre-existing heart disease, but in whom the time and mode of death are unexpected.

Gaziano JM in Braunwald, Zipes, Libby Heart Disease, 6th ed. W.B. Saunders 2001
There are various causes of sudden cardiac death in the post-MI population

<table>
<thead>
<tr>
<th>Arrhythmic cause:</th>
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<tbody>
<tr>
<td>• Ventricular tachycardia / fibrillation.</td>
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<tr>
<td>• Bradycardia.</td>
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<td>• Torsades de Pointes.</td>
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<tr>
<th>Non-arrhythmic cardiovascular cause:</th>
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<tr>
<td>• Recurrent myocardial ischemia.</td>
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<tr>
<td>• Pump failure.</td>
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<td>• Myocardial rupture.</td>
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<tr>
<td>• Stroke.</td>
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<td>• Pulmonary embolism.</td>
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| Non-cardiovascular cause           |
Sudden cardiac death in patients with coronary artery disease: Incidence

- Arrhythmia risk factors: ~5-10%
- Hemodynamic risk factors: ~7-15%
- Acute coronary syndrome: ≤20%
- First clinical event: ≥30%
- Known disease; low power or non-specific markers: ~33%

Sudden cardiac death is most common early after myocardial infarction: VALIANT trial

Solomon SD et al. *NEJM* 2010;352:2581-2588.
Causes of sudden death from myocardial infarction/rupture vs. presumed arrhythmic causes: Insights from the VALIANT trial

Sudden cardiac death due to ventricular arrhythmia in the post-MI population: pathophysiology

There are multiple mechanisms which contribute to the pathophysiology of SCD (due to VT/VF) in the post-MI population, including:

1) *Transient ischemia.*
2) *Acute myocardial infarction.*
3) *Scar-related pathophysiology.*
4) *Ischemic cardiomyopathy.*

Overview of the incidence and pathophysiology of sudden cardiac death (SCD) in the post-myocardial infarction (MI) population, with a particular emphasis on SCD related to ventricular arrhythmias (VF/VT).

1) In the post-MI population, the rates of sudden cardiac death are highest in the first 30 days.

2) Aside from arrhythmic causes of SCD, fatal MI / myocardial rupture are important causes of death in the early post-MI phase.

3) Impaired left ventricular ejection fraction (LVEF) is associated with increased risks of SCD in the post-MI population.

4) Myocardial ischemia, scar-related pathophysiology, and ischemic cardiomyopathy are important mechanisms of ventricular arrhythmogenesis in the post-MI population.
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3) Discuss areas of uncertainty/controversy in the use of ICD’s for SCD management amongst post-MI patients.
The role of primary prevention ICD in the reduction of SCD among patients with ischemic heart disease: RCTs

<table>
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<tr>
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<th>ICD</th>
<th>Control</th>
<th>Risk Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MADIT-I</td>
<td>15/95</td>
<td>39/101</td>
<td>0.41 (0.24, 0.69)</td>
</tr>
<tr>
<td>MADIT-II</td>
<td>105/742</td>
<td>97/490</td>
<td>0.71 (0.56, 0.95)</td>
</tr>
<tr>
<td>ScD-HeFT</td>
<td>120/431</td>
<td>161/453</td>
<td>0.78 (0.64, 0.95)</td>
</tr>
<tr>
<td>Total</td>
<td>240/1268</td>
<td>297/1044</td>
<td>0.67 (0.51, 0.88)</td>
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Implantation of primary prevention ICD’s conferred a survival benefit amongst patients with ischemic heart disease and depressed LVEF.

In all 3 trials, the majority of patients (>75%) had their most recent MI occurring ≥ 6 months from study randomization.

### Primary prevention ICD indications in the post-MI population: Canadian perspective

#### Class I

Patients with ischemic heart disease with or without mild-to-moderate heart failure symptoms and LVEF ≤ 30%, measured at least 1 month post-MI or 3 months after coronary revascularization (CABG or PCI).

#### Class IIA

Patients with ischemic heart disease and LV dysfunction (LVEF 31-35%), measured at least 1 month post-MI or 3 months after coronary revascularization with inducible VF or sustained VT during electrophysiology study.

Primary prevention ICD implant in post-MI patients: US perspective

<table>
<thead>
<tr>
<th>Class 1 (level of evidence: A)</th>
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<tbody>
<tr>
<td>With LVEF ≤ 35% due to prior myocardial infarction (MI) who are at least 40 post days post-MI and who are in NYHA II or III.</td>
</tr>
<tr>
<td>With LV dysfunction due to prior MI who are at least 40 days post-MI, have a LVEF ≤ 30%, and are in NYHA I.</td>
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<tr>
<th>Class 1 (level of evidence: B)</th>
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<tr>
<td>With non-sustained VT due to prior MI, LVEF &lt; 40%, and inducible VF or sustained VT at electrophysiological study.</td>
</tr>
</tbody>
</table>

Tracy CW et al. *Circulation* 2012;126:1784-1800.
What is the role of primary prevention ICD implantation in the early (≤ 40 days) post-MI period?

- Both the DINAMIT and IRIS trial randomized patients with reduced LVEF to receive ICD versus no ICD in the early post-MI period (≤ 40 days and ≤ 31 days, respectively).

- In both trials, there was no difference in all-cause mortality between the ICD and no ICD group.

In both the DINAMIT and IRIS trial, subjects in the ICD group had lower rates of arrhythmic/sudden cardiac death when compared to the no ICD group.

However, these subjects had higher rates of non-arrhythmic/non-sudden cardiac death when compared to the no ICD group.

“Conversion of death mode” hypothesis.

When to implant an ICD in the post-MI patient?

The “48-hour” and “40-day” concept

- **< 48 hours**
  - It is generally “accepted” that ventricular arrhythmias (including sustained VT or VF) occurring within 48 hours of the index MI are not associated with increased risks of recurrence SCD during later follow-up.

- **48 hours to 40 days**
  - The role of primary prevention (“prophylactic”) ICD implant is not proven.
  - ICD is indicated for secondary prevention if sustained VT/VF occurs in the absence of recurrent ischemia.

- **> 40 days**
  - Primary prevention (“prophylactic”) ICD implant is indicated in the presence of persistently depressed LVEF (≤30%), optimal medical therapy, and reasonable expectation for survival with a good functional status.

Pathways of sudden cardiac death: Conceptual diagram

- **Myocardial ischemia**
  - VF / VT
  - SCD

- **Heart failure**
  - VF / VT
  - SCD

ICD

"Primary VF/VT"

"Secondary VF/VT"

"Secondary VF/VT"
Prevention of sudden cardiac death: Importance of “upstream” therapies

Timely + effective reperfusion therapy

Myocardial ischemia

↑ Heart failure

Beta-blockade
ACE inhibition
Aldosterone antagonism

ICD

VF / VT → SCD

“Primary VF/VT”

VF / VT → SCD

“Secondary VF/VT”

VF / VT → SCD

“Secondary VF/VT”

Gibson CM et al. JACC 2008;51:546-551.
Hjalmarsen Å. AJC 1997;80(9B):35J-39J.
Summary statements: objective #2

Review of the role of implantable cardioverter defibrillators (ICD) in the management of sudden cardiac death amongst patients with ischemic heart disease.

1) Amongst medically-optimized post-MI patients with impaired LVEF (≤ 30%), primary prevention (“prophylactic”) ICD implantation is associated with improved survival.

2) Early (≤ 40 days) implantation of primary prevention ICD’s does not confer a survival benefit in the post-MI population.

3) Remember that timely + effective reperfusion therapies, beta-blockade, ACE inhibition, and aldosterone antagonism agents can reduce rates of SCD in the post-MI population.
Objectives

1) Overview of the incidence and pathophysiology of sudden cardiac death (SCD) in the post-myocardial infarction (MI) population, with a particular emphasis on SCD related to ventricular arrhythmias (VF/VT).

2) Review the role of implantable cardioverter defibrillators (ICD) in the management of sudden cardiac death amongst patients with ischemic heart disease.

3) Discuss areas of uncertainty/controversy in the use of ICD’s for SCD management amongst post-MI patients.
Some areas of uncertainty / controversy in the use of ICD’s for prevention of SCD in post-MI patients

1) Is there a role for diagnostic EP testing (for inducible VT) in risk stratifying post-MI patients for sudden cardiac death?

2) Can (timely) reperfusion therapy alter one’s propensity for developing subsequent VT / VF?

3) Can catheter-based VT ablation obviate the need for subsequent ICD implantation in at-risk patients?
Is there a role for EP study in the early post-MI phase for patients with LV dysfunction?

- Patients with LVEF ≤30% or ≤35% with heart failure symptoms underwent diagnostic EP study for inducible VT early post-MI (median: 14 days).
- If the EPS was negative for inducible VT, ICD’s were not implanted.

The 3-year rates of death or arrhythmia were comparable between the 2 groups.

| LVEF >40% | 1286 | 912 | 285 |
| LVEF ≤35%, EP- | 80 | 57 | 31 |
The potential importance of reperfusion therapy on subsequent rates of ICD therapies for VT/VF

Can catheter-based VT ablation obviate the need for subsequent ICD implantation in at-risk patients?

Foregoing ICD implantation in patients presenting with ventricular tachycardia: Is catheter ablation alone sufficient?

Erik Wissner and Karl-Heinz Kuck*

Retrospective, multicenter cohort of 166 patients with structural heart disease (55% ischemic), LVEF > 30%, and sustained monomorphic VT who underwent VT ablation. *These patients did not receive ICD’s at the outset.*


* 11 patients eventually received ICD due to recurrent VT post-ablation.
Summary statements: objective #3

Discuss areas of uncertainty/controversy in the use of ICD’s for SCD management amongst post-MI patients.

1) Diagnostic EP study for inducible VT may be a useful risk stratification tool for post-MI patients. Absence of inducible VT may define a lower-risk subset of patients who may not warrant prophylactic ICD therapy, despite having impaired LVEF.

2) The myocardial substrate which presumably potentiates VT/VF is substantially different between reperfused vs. non-reperfused patients. This may alter one’s propensity for developing future VT/VF.

3) In some patients, VT ablation may potentially obviate the need for subsequent ICD implantation – this may be particularly relevant for those with preserved LVEF and is the subject of ongoing research.
Conclusions: 3 Key messages

1) The incidence of sudden cardiac death (SCD) after myocardial infarction (MI) is highest in the early phase (<30 days). Ventricular arrhythmias (VT/VF) and recurrent ischemia are important causes of SCD during this early period. Over time, ventricular arrhythmia becomes increasingly important as a cause for SCD in post-MI patients.

2) The 4 main pathophysiological causes of SCD due to ventricular arrhythmia include: i) transient ischemia; ii) acute MI, iii) LV scar, and iv) adverse LV remodelling due to ischemic cardiomyopathy. As such, treatments directed at these underlying mechanisms are highly relevant in the prevention of SCD.

3) The use of primary prevention (“prophylactic”) implantable cardioverter defibrillators (ICD) confers a survival benefit in post-MI patients with depressed LVEF’s. However, randomized clinical trials did not suggest a benefit for early (<40 days) ICD implantation in high-risk, post-MI individuals.
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Thank you for your attention

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