Vasospastic Angina Manifesting as Aborted Sudden Cardiac Death

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Long-term Prognosis of Variant angina

- Yasue H et al, Circ 1988 -

- 245 patients with variant angina
- Average F/U : 80.5 months (range, 36–184 months)
- Survival rate at 10 years : 93%
- Use of calcium antagonists!!
Variant Angina Manifesting As ASCD

Q1. What is Prognosis?
Q2. How to Treat: ICD?
Aborted SCD patient in 2006...

- YS Lee (52/M)
  - 2006. 5~6. intermittent chest pain
  - 2006. 6. 7. sleeping after drinking with dinner
    → 6. 8. 06:30AM severe chest pain with radiation to neck after voiding
    → syncope
    → ER via 119 : at arrival, apnea and ventricular fibrillation
    → Defibrillation
YS Lee (52/M)

- His consciousness recovered
- 2006. 6. 12. CAG : 20-30% mild stenosis in LAD and LCx
- Ergonovin provocation :
  total occlusion in LAD with chest pain
- 2006.6.16. ICD implantation
52YO/Male, Aborted Sudden Cardiac Death
Ergonovine Provocation CAG
However, Finally….

• Korea Health Insurance Review & Assessment Service (H.I.R.A) did not reimburse this ICD procedure, even with administrative litigation (行政訴訟)

• After this decision, Korean EP physicians cannot implant ICD in patients with variant angina manifesting as aborted sudden cardiac death and have to prescribe medication first!!
Q1. What is Prognosis?

What is known:

Favorable long-term outcomes

Poor clinical outcomes

• Controversial results
• The limited number of patients and short F/U.
Q2. How to Treat: ICD?

**Guideline of ICD**

- ICD therapy is indicated in patients who are survivors of cardiac arrest due to ventricular fibrillation or hemodynamically unstable sustained ventricular tachycardia after evaluation to define the cause of the event and to **exclude any completely reversible causes**.

- Coronary Spasm: Completely reversible Cause?

*Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities J Am Coll Cardiol 2008;51:e1-62*
Arrhythmic Cardiac Arrest Due to Isolated Coronary Artery Spasm: Long-Term Outcome of Seven Resuscitated Patients

Philippe Chevalier MD, Antoine Dacosta MD, Pascal Defaye MD, Thierry Chalvidan MD, Eric Bonnefoy MD, Gilbert Kirkorian MD, Karl Isaaz MD, Bernard Denis MD, Paul Touboul MD

Results. The patients’ mean age was 44 years; three were male and four female. All were habitual cigarette smokers. No arrhythmias were induced on programmed ventricular stimulation; corrected QT interval (QTc) and corrected JT interval (JTC) dispersion were within normal ranges. After the ergonovine provocation test, treatment with calcium a dose determined by titration until a negative test result was obtained. At a mean follow-up interval of 58 months for the total group, six patients remained free of symptoms, whereas the one patient who did not stop smoking had a new cardiac arrest despite treatment for coronary spasm.

Conclusions. A favorable long-term outcome may be expected in survivors of cardiac arrest due to coronary spasm, in the absence of significant coronary artery disease. Calcium channel blockers are the most appropriate therapy in these patients. These observations provide further evidence for the role of silent ischemia in cardiovascular death.
Diagnosis and management of out-of-hospital cardiac arrest secondary to coronary artery spasm

- Among 300 OHCA, spasm demonstrated and survived after 1 month: 6/10 pts
- New provocation test at 1m → spasm occurred in 5 with CCB
- Coronary stenting(2), ICD(1), ↑ Tx drug dose(2)
- No cardiac arrest after 55±27 months

**Conclusions:**
- Frequent residual spasm despite CCB
- **Repetitive provocation test-guided Tx recommended**
Favorable outcomes of patients with vasospastic angina associated with cardiac arrest

Yoshihiro Yamashina (MD, PhD), Tetsuo Yagi (MD, PhD)*, Akio Namekawa (MD),

- 18 consecutive vasospastic angina with cardiac arrest, 17 discharged without Cx
- 1 patient died of cancer 50 months after arrest
- **All patients(16) alive w/o V. arrhythmia, syncope, cardiac arrest during mean F/U of 67 months**
  - quit smoking, long-acting CCBs ± nitrates
- ICD implanted in 6 : no ventricular arrhythmias
N=8 (ICD in 7)
- Survival from documented VF
- Normal CAG with evidence of coronary spasm
- Recurrent angina Sx despite medical Tx

5/8 patients had VA events

Inappropriate shock
Out-of-hosp. VF → died without ICD
Clinical Implications of an Implantable Cardioverter-Defibrillator in Patients With Vasospastic Angina and Lethal Ventricular Arrhythmia

Yuya Matsue, MD,* Makoto Suzuki, MD, PhD,* Mitsuhiro Nishizaki, MD, PhD,† Rintaro Hojo, MD,‡ Yuji Hashimoto, MD, PhD,* Harumizu Sakurada, MD, PhD‡ Chiba, Kanagawa, and Tokyo, Japan

(J Am Coll Cardiol 2012;60:908-913)

Results

Twenty-three patients were included in the present study and completely followed up. All patients are still alive. During a follow-up of 2.9 years (median 2.1 years), 4 ventricular fibrillations and 1 episode of pulseless electrical activity occurred in 5 patients (21.7%). There were no statistically significant differences in patient characteristics between the recurrence and nonrecurrence groups, including medication, smoking status, and whether the

Conclusions

Patients with VSA and lethal ventricular arrhythmia are a population at high risk for recurrence of cardiopulmonary arrest, and there is no reliable indicator for predicting recurrence of ventricular arrhythmia. Insertion of an ICD with medication for VSA is appropriate for this high-risk population. (J Am Coll Cardiol 2012;60:908-913)
Clinical Characteristics and Long-Term Prognosis of Vasospastic Angina Patients Who Survived Out-of-Hospital Cardiac Arrest (Circ EP. 2011;4:295-302.)

Multicenter Registry Study of the Japanese Coronary Spasm Association

- MACE free: 72% vs 92% at 5 yrs
- ICD shock: 2/14 pts
- Survival: 97 vs 98%

* MACE: cardiac death, nonfatal MI, hospitalization for unstable angina pectoris and heart failure, and appropriate ICD shocks
## Table 3

Correlated Factors for MACE in VSA Patients and Assigned Score

*(J Am Coll Cardiol 2013;62:1144-53)*

<table>
<thead>
<tr>
<th></th>
<th>Univariable Analysis</th>
<th></th>
<th>Multivariable Analysis</th>
<th></th>
<th>Assigned Score</th>
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<tbody>
<tr>
<td></td>
<td>HR</td>
<td>95% CI</td>
<td>p Value</td>
<td>HR</td>
<td>95% CI</td>
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<tr>
<td>Age</td>
<td>0.99</td>
<td>0.97-1.01</td>
<td>0.38</td>
<td>1.17</td>
<td>1.04-2.79</td>
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<tr>
<td>Male</td>
<td>1.07</td>
<td>0.64-1.79</td>
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<td>Hypertension</td>
<td>0.90</td>
<td>0.58-1.38</td>
<td>0.62</td>
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<td>Dyslipidemia</td>
<td>1.17</td>
<td>0.76-1.79</td>
<td>0.48</td>
<td>1.54</td>
<td>0.95-2.50</td>
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<tr>
<td>Diabetes mellitus</td>
<td>1.57</td>
<td>0.94-2.61</td>
<td>0.09</td>
<td>1.71</td>
<td>1.04-2.79</td>
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<td>Smoking</td>
<td>1.96</td>
<td>1.21-3.19</td>
<td>0.006</td>
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<td>Previous myocardial infarction</td>
<td>2.19</td>
<td>1.10-4.38</td>
<td>0.026</td>
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<tr>
<td>Angina at rest alone</td>
<td>1.49</td>
<td>0.95-2.35</td>
<td>0.09</td>
<td>1.71</td>
<td>1.08-2.72</td>
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<tr>
<td>ST-segment elevation during angina attack</td>
<td>1.50</td>
<td>0.93-2.42</td>
<td>0.09</td>
<td>1.54</td>
<td>0.95-2.50</td>
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<tr>
<td>History of OHCA</td>
<td>3.98</td>
<td>1.73-9.13</td>
<td>0.001</td>
<td>3.79</td>
<td>1.61-8.94</td>
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<tr>
<td>Significant organic stenosis</td>
<td>2.28</td>
<td>1.39-3.73</td>
<td>0.001</td>
<td>2.24</td>
<td>1.33-3.78</td>
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<tr>
<td>LAD spasm</td>
<td>1.28</td>
<td>0.81-2.02</td>
<td>0.29</td>
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<td>LCx spasm</td>
<td>1.16</td>
<td>0.75-1.80</td>
<td>0.50</td>
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<td>RCA spasm</td>
<td>1.05</td>
<td>0.68-1.61</td>
<td>0.83</td>
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<tr>
<td>Multivessel spasm</td>
<td>1.51</td>
<td>0.94-2.45</td>
<td>0.09</td>
<td>1.69</td>
<td>1.03-2.78</td>
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<tr>
<td>Calcium-channel blocker</td>
<td>0.73</td>
<td>0.35-1.51</td>
<td>0.39</td>
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<tr>
<td>Long-acting nitrate</td>
<td>1.35</td>
<td>0.89-2.07</td>
<td>0.17</td>
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<td>Antiplatelet</td>
<td>1.43</td>
<td>0.94-2.20</td>
<td>0.10</td>
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<tr>
<td>Beta-blocker</td>
<td>2.34</td>
<td>1.08-5.06</td>
<td>0.032</td>
<td>2.00</td>
<td>0.88-4.54</td>
</tr>
</tbody>
</table>
Clinical Risk Score Developed by the Japanese Coronary Spasm Association (J Am Coll Cardiol 2013;62:1144-53)

Median F/U : 32 months, ICD : 14/35 patients with OHCA, appropriate shock in 2
Objective

• To evaluate the long-term risk of mortality and ventricular tachy-arrhythmic events of variant angina patients with ASCD compared with those without ASCD

• To compare cardiac mortality between patients who received ICD implantation or not in ASCD patients
Patients

Between March 1996 and September 2014, 188 variant angina patients with ASCD and 1844 variant angina without ASCD were retrospectively enrolled from 13 heart centers in South Korea.

Inclusion criteria in ASCD group

1. Cardiac arrest due to VT/VF or PEA
2. Successfully resuscitated
3. Documented coronary spasm
4. No organic heart disease

Inclusion criteria in No-ASCD group:

Provocation test positive with chest pain
Outcomes

• Primary endpoint: Cardiac Death
  (Any death due to proximate cardiac cause, including cardiac arrest, MI, low-output failure, fatal arrhythmia)

• Secondary endpoint
  - Death from any cause
  - Ventricular tachy-arrhythmia
  - Appropriate ICD treatment

J Am Coll Cardiol 2016;68:137–45
## Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>With ASCD (n=188)</th>
<th>Without ASCD (n=1844)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age – yr</td>
<td>52.8±9.9</td>
<td>55.3±9.5</td>
<td>0.001</td>
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<tr>
<td>Male sex – no. (%)</td>
<td>143 (76.1)</td>
<td>1427 (77.4)</td>
<td>0.68</td>
</tr>
<tr>
<td>Hypertension – no. (%)</td>
<td>64 (34.0)</td>
<td>914 (49.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes – no. (%)</td>
<td>15 (8.0)</td>
<td>190 (10.3)</td>
<td>0.31</td>
</tr>
<tr>
<td>Smoking – no. (%)</td>
<td>103 (54.8)</td>
<td>900 (48.8)</td>
<td>0.12</td>
</tr>
<tr>
<td>Hyperlipidemia – no. (%)</td>
<td>27 (14.4)</td>
<td>560 (30.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Family history – no. (%)</td>
<td>5 (2.7)</td>
<td>16 (0.9)</td>
<td>0.021</td>
</tr>
<tr>
<td>ST-segment elevation</td>
<td>102 (54.3)</td>
<td>509 (27.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Multivessel spasm – no. (%)</td>
<td>32 (17.0)</td>
<td>171 (9.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>Ejection fraction – %</td>
<td>60.6±9.9</td>
<td>62.5±5.4</td>
<td>0.01</td>
</tr>
<tr>
<td>Number of type of vasodilator</td>
<td>2.6±0.9</td>
<td>2.3±0.8</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
RESULTS: Cardiac Death

Adjusted HR: 7.26 (4.21-12.5), P<0.05

Incidence Rate (per 1000 person-yrs)

24.1 vs. 2.7

Patient at risk

without cardiac arrest with cardiac arrest

Years

0 1 2 3 4 5 6 7 8 9 10

Cumulative Incidence, %

0 10 20 30 40 50

1844 1649 1412 1163 867 580

0.8% 1.3% 1.7% 2.1% 2.5%

7.7% 11.5% 12.8% 16.7% 16.7%

ASCD (+) ASCD (-)

J Am Coll Cardiol 2016;68:137–45
Death from any cause

Adjusted HR: 3.00 (1.92-4.67), P<0.05

Incidence Rate (per 1000 person-yrs)

27.5 vs. 9.6

J Am Coll Cardiol 2016;68:137–45
Ventricular Tachyarrhythmia in patients with ASCD

Incidence Rate: 32.4 Per 1000 person-yrs

J Am Coll Cardiol 2016;68:137–45
Cardiac Death or Ventricular Tachyarrhythmia in patients with ASCD

Incidence Rate: **44.9** Per 1000 person-yrs

J Am Coll Cardiol 2016;68:137–45
Mortality in ASCD pts, ICD Implantation +/-

P = 0.15

Cumulative Incidence, %

Years

Patient at risk

ICD (-) ICD (+)

0 1 2 3 4 5 6 7 8 9 10

ICD (-) ICD (+) Appropriate ICD treatment

19.3%

4.3%

J Am Coll Cardiol 2016;68:137–45
In our present study, we found that variant angina patients with ASCD had higher rates of cardiac death and death from any cause than non-ASCD patients, despite successful resuscitation and treatment with multiple vasodilator therapies.

ASCD patients also had a high recurrence rate of ventricular tachyarrhythmia.

ASCD patients who underwent ICD implantation frequently received appropriate ICD treatment and had a non-significant trend of lower rate of cardiac death compared with patients without ICD implantation.
ICD + OMT versus OMT In Patients with Variant Angina Manifesting as Aborted Sudden Cardiac Death

VARIANT-ICD Trial

Patients with Variant Angina Manifesting as ASCD
1) Cardiac arrest due to documented VF, sustained VT
2) Successfully resuscitated without poor neurologic outcome
3) Variant angina diagnosed by coronary angiography
4) No organic heart disease associated with sudden cardiac arrest

ICD implantation on the top of optimal medical therapy (N=70)

Optimal medical therapy alone (N=70)

Primary endpoint at 5 years: Death from any cause

ClinicalTrials.gov Identifier: NCT02845531 (20 centers in KOREA)
Eligible For the Trial

- < 6months of randomization
- Documented VF or rapid VT
- Documented coronary spasm
  - Spontaneous spasm with STE
  - **Positive provocation CAG**: The definition of positive result is *total or subtotal (>90% luminal diameter narrowing) occlusion* in ergonovine provocation coronary angiography
- No other heart diseases associated with sudden cardiac death
Primary Outcome

- Death from any cause at the 5 years of follow-up

Secondary Outcome

- Cardiac death, Death from arrhythmia
- Cardiac arrest defined as sudden loss of consciousness requiring direct-current
- Recurrence of ventricular tachyarrhythmia (ventricular tachycardia or fibrillation)
- Appropriate ICD therapies defined as device-administered antitachycardia or defibrillation treatment for ventricular tachyarrhythmia
- Inappropriate ICD therapies
Thank you for your attention!