A novel clinical risk prediction model for sudden cardiac death in HCM: a proof of concept study

C O’Mahony,* S Rahman,** E Biagini,† C Rappezzi,† L Monseratt,‡ J Gimeno,¶ G Limongeli, § A Anastasakis,‖ W McKenna,* P Elliott.*

*Inherited Cardiac Diseases Unit, The Heart Hospital/University College London, London, United Kingdom
** Department of Statistics, University College London
† Institute of Cardiology, University of Bologna, Bologna, Italy
‡ Complejo Hospitalario Universitario, Juan Canalejo, Coruna, Spain
¶ University Hospital Virgen de la Arrixaca, Murcia, Spain
§ Monaldi Hospital, Second University of Naples, Naples, Italy First Department of Cardiology
‖ University of Athens, Heart Center of the Young and Athletes, Unit of Inherited Cardiovascular Diseases, Athens, Greece
Overview

- SCD in HCM
- Review of current management
- Outcomes of patients treated with ICD
- Accuracy of current risk stratification
- Novel risk prediction model for SCD
Hypertrophic cardiomyopathy
SCD in HCM

Electrograms:

Atrial
Ventricular
Shock lead

Atrial
Ventricular
Shock lead

C O’Mahony et al; Europace 2012
Which patients should receive an ICD for the primary prevention of SCD?
Risk factors of SCD

- Non-sustained ventricular tachycardia
- Family history of SCD
- Syncope
- Severe LVH (LV Wall Thickness ≥30mm)
- Abnormal blood pressure response to exercise

C O’Mahony et al; Circ AE in press
ACC/ESC 2003 & ACCF/AHA 2011 guidelines

≥2 risk factors = ICD

1 risk factor = ?
ACCF/AHA: ICD for FHSCD/LVH/Syncope

0 risk factors = Reassure

B Maron et al; EHJ 2003 & B Gersh et al; JACC 2011
What is the experience of patients treated with ICDs according to ACC/ESC 2003 guidelines?
Low incidence of appropriate therapies

C O’Mahony et al; Heart 2012
High prevalence of complications

n=334

Adverse events: 27%

Appropriate shock & complication: 3%

Appropriate shock without adverse event: 6%

No events: 64%

C. O'Mahony et al; Heart 2012
How good are the current risk factors and ACC/ESC 2003 algorithm in distinguishing high from low risk patients?
Discrimination of ACC/ESC 2003 algorithm

\[ \text{ROC(t) AUC} = 0.64 \text{ at 5 years} \]
Is there a better alternative to SCD risk stratification?
Risk prediction models

• Mathematical functions that mimic natural processes

• Cox Proportional Hazards Model:

\[
\sum_{i=1}^{k} \beta_i X_i
\]

\[
h(t, X) = h_0(t) e^{\sum_{i=1}^{k} \beta_i X_i - \sum_{i=1}^{k} \beta_i \bar{X}_i}
\]

• Probability for an end-point at a specific time point:

\[
\hat{P} = 1 - S_0(t) e^{\sum_{i=1}^{k} \beta_i X_i}
\]
Model development

The Heart Hospital, London

- 1643 patients ≥16 years
- 12 244 patient-years
- 93 SCD end-points
- 5-year cumulative survival:
  - 96% (95% CI 94.0-98.0)
CANDIDATE PREDICTORS

Demographic
  • Age

Historical
  • Syncope
  • Family history of SCD

ECG Holter
  • Atrial fibrillation
  • NSVT

Echo
  • MWT
  • LV diastolic size
  • LVOT gradient
  • LA size
Model fitting

- Backward selection

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>HR</th>
<th>HR 95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>-0.0160781</td>
<td>0.9840505</td>
<td>0.967 - 1.001</td>
<td>0.069</td>
</tr>
<tr>
<td>NSVT</td>
<td>0.8089973</td>
<td>2.245655</td>
<td>1.413 - 3.569</td>
<td>0.001</td>
</tr>
<tr>
<td>Log (MWT), mm</td>
<td>0.66825</td>
<td>1.95082</td>
<td>0.886 - 4.296</td>
<td>0.097</td>
</tr>
<tr>
<td>LA, mm</td>
<td>0.0434312</td>
<td>1.044388</td>
<td>1.016 - 1.074</td>
<td>0.002</td>
</tr>
<tr>
<td>Syncope</td>
<td>0.6342903</td>
<td>1.885683</td>
<td>1.163 - 3.058</td>
<td>0.010</td>
</tr>
<tr>
<td>FHSCD</td>
<td>0.66825</td>
<td>1.678682</td>
<td>1.070 - 2.633</td>
<td>0.024</td>
</tr>
</tbody>
</table>

- Probability of SCD at 5 years=

\[1 - 0.99937 \exp^{(1.4854 + \text{Age} \times -0.0176 + \text{NSVT} \times 0.887 + \log(\text{MWT}) \times 0.782 + \text{LA} \times 0.0413 + \text{Syncope} \times 0.633 + \text{FHSCD} \times 0.4173 + \text{LVOTG} \times 0.00287)}\]
Model validation

Institute of Cardiology, Bologna

• 456 patients
• 2955 patient years
• 41 SCD end-points
• 5 year cumulative survival:
  – 94% (95% CI 91.1-95.5)
• Calibration:
  – agreement between observed and predicted probabilities of the model was 82%
• Discrimination:
  – ability to distinguish between those with SCD and those without the outcome
  – Harrell's c test: 78%
Clinical application

Asymptomatic
MWT 25mm
NSVT
Moderate LA dilation

22 year old
LVOT gradient 70mmHg

56 year old
LVOT gradient 28mmHg

Current guidelines treat these 2 patients the same

5-year SCD probability: 12%
5-year SCD probability: 4%
Web-based risk calculators: euroSCORE

Important: The previous additive and logistic EuroSCORE models are out of date. A new model has been prepared from fresh data and is launched at the 2011 EACTS meeting in Lisbon. The model is called EuroSCORE II. This online calculator has been updated to use this new model. If you need to calculate the older “additive” or “logistic” EuroSCORE please visit the old calculator by clicking here.

<table>
<thead>
<tr>
<th>Patient related factors</th>
<th>Cardiac related factors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong> 1 (years)</td>
<td><strong>NYHA</strong></td>
</tr>
<tr>
<td></td>
<td><strong>CCS class 4 angina</strong></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>select 2</td>
<td>select 8</td>
</tr>
<tr>
<td><strong>Renal impairment</strong> 2</td>
<td></td>
</tr>
<tr>
<td>normal (CC &gt;85ml/min)</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>LV function</strong></td>
</tr>
<tr>
<td><strong>Extracardiac arteriopathy</strong> 3</td>
<td></td>
</tr>
<tr>
<td>no 3</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Recent MI</strong> 9</td>
</tr>
<tr>
<td><strong>Pulmonary hypertension</strong> 10</td>
<td></td>
</tr>
<tr>
<td>no 4</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Operation related factors</strong></td>
</tr>
<tr>
<td><strong>Previous cardiac surgery</strong></td>
<td></td>
</tr>
<tr>
<td>no 5</td>
<td><strong>Urgency</strong> 11</td>
</tr>
<tr>
<td><strong>Chronic lung disease</strong> 5</td>
<td></td>
</tr>
<tr>
<td>no 5</td>
<td><strong>体重 of the intervention</strong> 12</td>
</tr>
<tr>
<td><strong>Active endocarditis</strong> 6</td>
<td></td>
</tr>
<tr>
<td>no 6</td>
<td>isolated CABG 12</td>
</tr>
<tr>
<td><strong>Critical preoperative state</strong> 7</td>
<td></td>
</tr>
<tr>
<td>no 7</td>
<td></td>
</tr>
<tr>
<td><strong>Diabetes on insulin</strong></td>
<td></td>
</tr>
<tr>
<td>no</td>
<td></td>
</tr>
</tbody>
</table>

EuroSCORE II 11

**Operational Factors**:
- **Urgency**: elective
- **Weight of the intervention**: isolated CABG
- **Surgery on thoracic aorta**: no

Notes: This is the 2011 EuroSCORE II.
Conclusions

• Current SCD risk stratification is suboptimal
• SCD risk prediction model provides risk predictions:
  – Validated
  – Accurate
  – Personalised prognostication
Acknowledgments

Supervision:
- Dr P Elliott (UCL)
- Prof W McKenna (UCL)
- Dr P Lambiase (UCL)
- Prof Rappezi (Bologna, Italy)
- Dr E Biagini (Bologna, Italy)
- Dr R Omar (UCL Statistics)
- Dr S Rahman (UCL Statistics)
- Dr A Pantazis (Heart Hospital)
- Dr M Tome-Esteban (Heart Hospital)
- Dr Juan Gimeno (Murcia, Spain)

Heart Hospital Inherited Cardiac Diseases team:
- Drs M Cardona, C Tang, M Calgagnino, G Quarta, A Muir, C Coats, C Critoph, V Patel, K Tsovolas, D Sado, A Flett
- L Moss, M Baldini, S Waller, S Jenkins, S Dickie
Thank you
High complication rate

Appropriate shocks (12% at 5y)

Complications (47% at 5y)

Cumulative survival

Follow-up years

C O'Mahony et al; Heart 2012
ACC/ESC 2003 & ACCF/AHA 2011 guidelines

- ICD indicated for secondary prevention
- No risk factors = reassurance
- 2 or more risk factors = ICD justified/reasonable
- ACC/ESC 2003:
  - 1 risk factor = ICD on individual basis
- ACCF/AHA 2011:
  - Family history SCD/Syncope/LVH = ICD reasonable

ACC/ESC guidelines: EHJ 2003; ACCF/AHA guidelines: JACC 2011